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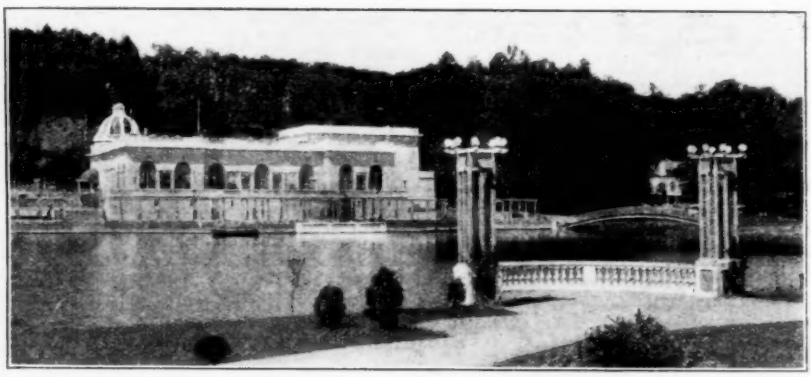

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CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT.

GOULSTONIAN LECTURES

on Polyuria. By Prof. E. B. VERNEY, F.R.C.P.
III.—Polyuria in Chronic Nephritis. —(*Illustrated*) 751

ORIGINAL ARTICLES.

The Administration of Insulin in Suspension. By O. LEYTON, F.R.C.P. —(*Illustrated*) 756
Pulmonary Neoplasms. By T. C. HUNT M.R.C.P. 759
Polycythæmia Vera Treated with Phenylhydrazine Hydrochloride. By W. MACKAY, M.B. —(*Illustrated*) 762
Pituitary Cachexia in Tabes Dorsalis. By T. S. GOOD, M.R.C.S., and K. O. NEWMAN, M.D. —(*Illustrated*) 765
Digestive Enzymes of the Human Foetus. By Prof. M. F. LUCAS KEENE, M.B., and E. E. HEWER, D.Sc.—(*Illustrated*) 767

CLINICAL AND LABORATORY NOTES.

Banisterine or Harmine. By Prof. J. A. GUNN, M.D., D.Sc. 769
The Preservation of Anæsthetic Ether. By C. LANGTON HEWER, M.B. . 770
Inhibitory Effect of a Staphylococcus Antivirus in Relation to pH of Medium. By R. F. HUNWICKE, B.Sc. 771

MEDICAL SOCIETIES.

Medical Society for the Study of Venereal Diseases: Venereal Disease in the Mercantile Marine 772
Royal Society of Medicine: War Section: Functional Nervous Disorders in the Services 773
British Psychological Society: The Psychopathology of Anxiety .. 774
Edinburgh Obstetrical Society: A Scheme of Maternity Service..... 776

REVIEWS AND NOTICES OF BOOKS.

Colour and Colour Theories. By Christine Ladd-Franklin 778
Neurosurgery. By Prof. William Sharpe, M.D., and Norman Sharpe, M.D. 778
Radiologia Clinica del Cuore e dei Grossi Vasi. By Prof. Cesare Pezzi... 779
La réduction des fractures sous écran radioscopique. By Dr. Radutzesco..... 779
Growth. By W. J. Robbins and others 779
Praktische Differentialdiagnostiek. By Dr. Albert Herz 779
Morphologic Variation and the Rate of Growth of Bacteria. By Prof. A. T. Henrici 779
Le Cancer Primitif du Poumon. By René Huguenin 780
A Panorama of Modern Civilisation. Edited by C. A. Beard..... 780
From the Seen to the Unseen. By John H. Best, B.Sc. 780

LEADING ARTICLES.

ON THE PASSING OF MUCH WATER 781
PUBLIC CLEANSING IN GREATER LONDON 781
CANCER OF THE LUNG.... 782

ANNOTATIONS.

The British Congress of Obstetrics and Gynæcology 783
The Flea at Sea..... 784
Oleothorax 784
Prognosis in Hay Fever .. 785
The Potato as Culture Medium 785
The Xanthoproteic Reaction in Renal Disease .. 785
Occupational Anæmias.... 786
The Metabolism of the Eskimo 786
Research on Anæsthesia .. 787
The Ophthalmological Society's Congress..... 787

CLINICAL INTERPRETATION OF AIDS TO DIAGNOSIS.

The Significance of Organisms in the Urine: I. Preliminary Tests for Infection. By LIONEL E. H. WHITBY, M.R.C.P. .. 788

SPECIAL ARTICLES.

The Evolution of Hospital Schools: Combined Treatment and Education for Children Suffering from Physical Defects. By Sir HENRY GAUVAIN, M.D., and EVELYN M. HOLMES, M.B.—(*To be concluded*) 789
Scotland: Aberdeen Joint Hospital Fund 792
Medicine and the Law: Overdose of Thallium Acetate: An Error in Calculation 795
Infectious Disease in England and Wales..... 795

CORRESPONDENCE.

Public Health Congress in Zurich (Drs. E. W. Hope and T. N. Kelynack).... 793
The Employment of Bacteria in Modern Warfare (Lord Moynihan) 793
Gallop Rhythm (Dr. F. G. Crookshank)..... 794
Blood Standards (Dr. C. E. Jenkins) 794
Hickman Memorial Fund (Dr. Cecil Hughes) 794
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OBITUARY.

Sir Anthony Bowlby.—(*With portrait*) 796
R. L. Mackenzie Wallis, M.D.—(*With portrait*) .. 797
Alexander Granville, M.R.C.S.—(*With portrait*) 798
William Louis Byham, M.R.C.S. 799

MEDICAL NEWS.

Royal College of Surgeons of Edinburgh 800
University of Aberdeen.. 800
University of Birmingham 800
Berkshire Contributory Scheme 762
A Poor-law Country Home 762
British Orthopædic Association..... 777
British Empire Cancer Campaign 777
Princess Mary at Bradford 787
Ancoats Hospital, Manchester 787
Salisbury Infirmary League 789
Donations and Bequests.. 799
Alcohol in Therapeutics... 799
Post-graduate Demonstrations at Birmingham .. 800
Post-graduate Course on Mental Deficiency..... 800
Bayliss-Starling Memorial Scholarship..... 800
Eugenics Society 800
Royal Society of Arts.... 800
Auxiliary Royal Army Medical Corps Funds.... 800
University of London Medical Graduates Society 800
Garton Prize and Medal.. 800
Clinic for Treatment of Rheumatism as Brighton 800
Treloar Hospitals and College 801

NOTES, COMMENTS, AND ABSTRACTS.

Pitfalls in the Right Side of the Abdomen. By H. W. CARSON, F.R.C.S. 802
Local Authorities and Maternal Deaths 804
Ultra-violet Apparatus.... 804
Uterine Fixation by Transplanted Fascia.... 804
Robb's Dietetic Biscuits.. 804

Medical Diary 801
Appointments 801
Vacancies 801
Births, Marriages, Deaths. 802

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LECTURE III.*—POLYURIA IN CHRONIC NEPHRITIS.

(Delivered on March 14th.)

MR. PRESIDENT AND FELLOWS,—In the first lecture emphasis was laid on the dependence of the kidney for its physiological conduct, in so far as its rapid and purposive response to an increased load of water in the tissues is concerned, on the secretory activity of the pituitary body. Such dependence may—we do not know—represent one aspect only of a fuller reliance by the kidney on the metabolic activities of the endocrine glands. But this much is clear—viz., that the water elimination by the normal kidney is profoundly influenced by the content of the blood in the secretory product of the pituitary gland. And, in that both when the secretion of the pituitary body is impaired by experimental interference and by the incursions of disease, the physiological background of the kidney must itself be sufficiently reactive in order that the typical response to the lowering of the pituitrin content of the blood may be made manifest, it is not surprising that there is close agreement between the findings of pathology and those of experimental physiology.

The interpretation of the polyuria which is seen to accompany certain forms of chronic nephritis seems in the present state of knowledge to be a much more difficult problem, and one feels acutely that anything one has to say on the subject is necessarily disjointed and speculative. But it may not be entirely without value if the clinical and pathological facts, as generally accepted at the present time, are first described, and then, in the light of our present knowledge of the physiology of the kidney and of the cardiovascular system, an attempt made to form some conception of the mechanisms responsible for the exhibition of these facts.

Polyuria is typically associated with those structural changes which are found in the so-called contracted white kidney. The glomeruli are extensively and unequally damaged, and show varying degrees of patency in the capillary loops. The tubules exhibit marked signs of degenerative changes, these changes being perhaps dependent on the degree of glomerular damage (Löhlein [9]). The structure of the kidney is extensively altered, depending partly on the destruction of the specific parenchyma, partly on regenerative processes. Polyuria, especially nocturnal polyuria, is often the first symptom of the disease, but "no close parallelism exists between the weight of the kidney, its appearance, and the amount of urine it secreted before death" (Osler [11]). And all attempts to correlate the degrees of structural change with the functional responses of such kidneys fail. But when the structural changes are intense the polyuria may be said to be obligatory, and raised arterial tension is persistent and extreme. The vasculature of the kidney shows extensive arteriosclerotic changes, but that these changes are secondary to the raised arterial tension is made unlikely by the fact that they may be strictly localised to the kidney or be at least much more extreme in their degree here than elsewhere in the body. The presence of such localised vascular changes in the kidney, associated as they are with high blood pressure, is an argument, as Volhard and Fahr [20] point out, in favour of their being connected as cause and effect. As already mentioned, nocturnal polyuria may be the first symptom of any derangement of renal function, and this may occur in the absence of any sign of a rise in the general blood pressure. On the other hand, high blood pressure is not necessarily associated with polyuria, as is well recognised in the fact that generalised arteriosclerosis, raised arterial tension, and cardiac hypertrophy are commonly encountered without there being any signs or symptoms of impairment in the function of the kidney. In such conditions the amount and colour of the urine may remain normal for many years, and the marked oscillations in the rate of urinary flow during the day, a phenomenon which above all others is to be regarded as a sign of normality in renal function, are as a rule conspicuously present. Quincke's [14] nycturia, it is true, is a symptom which is sometimes evident, but it is by no means invariably so. Tests of renal function, such as the water ingestion test, concentration tests involving the capacity of the kidney to excrete chloride or urea, give results which are commonly within the normal range—facts which are clearly to be associated with the retention of comparatively large amounts of normal renal tissue and with the frequency with which zones of hypertrophied parenchyma are met with. Such cases die not from renal insufficiency, but from causes due immediately to the structural or functional state of the cardiovascular system, whilst those afflicted with the diffuse chronic nephritis with which we are here mainly concerned die in latent or acute uræmia, or are prematurely carried off through the rupture of a cerebral blood-vessel. One pictures the "contracted white kidney" as arising from the continuous action on the kidney of some toxin locally or remotely produced, the "primary contracted kidney" as arising directly from a generalised vascular disease. Forms of kidney disease intermediate between these two main types may be encountered, but I think it would be generally agreed that in their purest forms these two types do exist and that clinically they may be readily recognised and differentiated.

The colour of the urine in the polyuria of chronic nephritis is pale, its specific gravity is low, ranging from 1005 to 1012, and the amount of albumin is variable, sometimes being hardly detectable, at other times abundant. Traces of blood are commonly present. The earliest functional change which can be detected in this progressive disease is the damping down of the normal variations in urinary output during the day. Hedinger and Schlayer [6] introduced a method of testing renal function which was based on this fact. The volume, specific gravity, and chloride content of the urine collected at two-hourly intervals during the day, and of that collected during the whole night, were measured. It was found that whereas in normal people there were wide variations in the figures relating to the specimens collected during the day, in chronic nephritis without œdema the curves showed a marked constancy in level throughout. The volume of urine was larger and such variations in the rate of urine flow as did occur were not reflected in any marked change in specific gravity or chloride content. In more severe cases there is an increase in the volume of the night urine, and when this occurs Hedinger and Schlayer state that there is widespread damage to the kidney parenchyma. But no definite relationship exists between the degree of structural damage to the kidney and its functional response. Mösenthal [10] repeated and extended the observations of Hedinger and Schlayer and made comparative tests of the effects of high and low protein diets in various forms of renal disease. It was found that nocturnal polyuria was much more frequent on the high than on the low diet, and it was concluded that when this symptom occurred with a low protein diet it was to be regarded as a much graver sign of renal insufficiency than when it occurred with a high. The nocturnal polyuria, as Volhard and Fahr [20] conclude, is to be regarded as a compensatory phenomenon.

* Lectures I. and II. appeared in THE LANCET of March 16th and 30th respectively.

When the capacity of the kidney to concentrate some specific substance such as urea or chloride is investigated it is found that such capacity is markedly diminished in severe or protracted forms of the disease, but that in the earlier stages, even when nocturnal polyuria is present, the capacity to deal with these substances may be to all intents and purposes normal. Tests involving the ingestion of a large volume of water and timing its rate of elimination may show a delayed excretion rate at a stage before that at which any marked impairment in the capacity of the kidney to eliminate urea is encountered. Later the incapacity to excrete large volumes of water rapidly ingested is very marked, and the immediate effect may be an actual diminution in the rate of water elimination (Mösenthal [10]). This incapacity to deal with large additional volumes of water is probably not unrelated to the fact that the polyuria of this disease does not respond to the administration of pituitrin (Hart [5c]). In this respect, then, it differs sharply from the polyuria of diabetes insipidus.

Blood analyses show an increase in the urea and in the non-urea non-protein nitrogen, and the value of these findings in forming an estimate of the degree of renal damage is very appreciable. The retention of other substances such as potassium, phosphate and creatinin in the blood of cases of chronic nephritis has also been reported, and reference will later be made to the significance of this retention. The disease may arise as a sequel to chronic parenchymatous nephritis, but quite commonly there is no history of dropsy, and the polyuria may, and quite commonly is, the first symptom of impaired renal function.

We may, then, sum up the clinical and pathological picture of chronic nephritis with polyuria as follows. In the earliest stage of the disease the first sign to be detected is a disappearance of those rapid swings in the rate of urine eliminated during the daytime which characterise health. Such a disappearance is accompanied or quickly followed by an increase in the volume of urine eliminated during the night. The quality of the urine tends towards a fixed and constantly maintained level in so far as its chloride content and specific gravity are concerned. Albumin is, and blood may be present. Water excretion, urea concentration, and chloride concentration tests, as well as the concentration of urea in the blood, may show little variation from the normal, and no rise in blood pressure may be detected.

As the disease progresses the polyuria becomes more marked, and tests for renal efficiency show that the capacity of the kidney to deal with a suddenly imposed load is waning. The amount of albumin and of blood in the urine is variable, and the urea content of the blood slowly goes up. The blood pressure rises and the rise is persistent. Later these signs and symptoms become more severe and death usually ensues from renal failure.

Our task, then, is to attempt to interpret in terms of physiological mechanisms with which we are already familiar, the signs of this disease and the course which it typically follows. The points which must particularly attract our attention are, in addition to the polyuria, the occasional absence of a raised blood pressure in the early stages, the marked and persistent rise which occurs in the later, the presence of albumin and blood in the urine, and the ingravescent fall in the capacity of the kidney to deal with any extra load to which it is subjected. Further, we must attempt to account for the absence of an increased urine flow in cases of essential hypertension and of generalised arteriosclerosis with high blood pressure.

Let us now turn to a consideration of those facts in the experimental physiology and pathology of urine secretion and of the cardiovascular system, which, so far as our present knowledge goes, may be considered to have an important bearing on the mechanisms behind the production of the polyuria and the course of the disease of which it forms so prominent a sign.

The first fact which I should like to emphasise is the enormous number of renal units which are packed together to form the human kidney. If we make a section tangential to the surface of the kidney we find that the medullary rays are represented as circular areas, the labyrinth of the kidney as the tissue intervening between them. If we examine such a section microscopically we find the medullary rays to be formed by the collecting tubules, whilst in the labyrinth immediately in contact with the medullary ray is a zone of convoluted tubules surrounded by a zone of glomeruli. Masses of such lobules are packed together to form the whole cortex. These lobules have been found to be structurally separable by Traut.[18] After maceration of pieces of human kidney tissue in 50 per cent. HCl for 8 to 12 hours he found that the lobules readily fell apart and that their structure could easily be investigated. The whole cortical surface of the lobule was clustered with glomeruli, inside which were packed the convoluted tubules which themselves formed a compact sheath around the cortical collecting ducts. It was possible to determine the number of these lobules in the human kidney, and by counting the number of glomeruli on the surface of several such units the approximate number of glomeruli in the whole kidney became known. This number is $4{\cdot}5 \times 10^6$, so that the normal man is provided with roughly 10 million units each potentially capable of supplying its quota of fully formed urine. That such an enormous number represents a considerable reserve of secretory tissue is indicated by the results of the experiments of Richards [15] and his colleagues.

Richards has shown by direct observation of the glomerular tufts of the frog's kidney that the number of active glomeruli—i.e., those through which a flow of blood is visible—varies continuously, and that the number of active glomeruli in a given field can be increased by injections of diuretic substances and diminished by injections of vasoconstrictor substances. Further, Richards has demonstrated the possibility, under the microscope, of puncturing the capsule of a glomerulus with a fine quartz pipette and of withdrawing by this means fluid from Bowman's space. The fluid flowed up the pipette only so long as blood was observed to pass through the glomerular capillaries. If these were touched with the point of the pipette they contracted down and the flow of fluid ceased. It would seem, then, that the secretory work of a renal unit was dependent on the flow of blood through its glomerulus.

Two results accruing from these experiments are of special interest to us at this juncture—namely, the alternation in the flow of blood through the glomerular tufts, and the cessation of the flow of fluid collected from Bowman's capsule when the blood flow through that glomerulus ceases. Each unit passes through alternate periods of rest and activity, and as we should perhaps expect, these interruptions are not regular in occurrence and do not affect all the glomeruli within a single field at the same time. The number of units is so large that it is possible for the kidney as a whole to function efficiently under normal conditions when each unit composing it works for a fraction only of its time. Such experiments give us a clearer insight into the meaning of the term "reserve of the kidney," since clearly, when increased work is called for, the units simply respond either by increasing their intervals of work at the expense of their intervals of repose, or by increasing the intensity of their work during their active periods. This alternation of activity and rest which the units of the kidney undergo may be looked upon as the concrete representation of its first line of defence against the inroads of disease.

We have already emphasised the dependence of the urine flow on the pressure stimulus. It does not necessarily follow that a rise in general blood pressure causes an increase in urine flow. Stimulation of the splanchnic nerve, for example, inhibits or arrests the flow of urine since the vasa afferentia are constricted and the pressure stimulus withheld from the glomeruli. The seat at which the pressure stimulus becomes effective—viz., the glomerulus—being situated between the vasa afferentia and the vasa efferentia can, by means of

a differential dilatation or constriction of these vessels, become exposed theoretically to any blood pressure from zero up to a value approximating to that of the general arterial pressure. This possibility of an enormous variation in glomerular pressure gives to the kidney its second intrinsic line of defence. But whereas in the calling up of its first reserves the composition and quantity of the urine would not necessarily be altered, immediately the second reserves are called into play an increased urine flow occurs accompanied by an approach in its composition towards that of the plasma. The degree of this approach is to be regarded as being determined by the "tone" of the individual units just as the degree of dilatation of the heart when subjected to an increased load is dependent upon the efficiency with which the extra work is performed. We saw in the last lecture two illustrations of this mobilisation of the second reserves of the kidney. In Rose Bradford's experiments a polyuria supervened, the degree of the polyuria in the non-fatal cases being roughly proportional to the amount of kidney substance removed.

Attempts to prove the results obtained by Rose Bradford [4] in his experiments on the reduction of the renal tissue have been undertaken by Bainbridge and Beddard,[2] and by Pearce.[12] Bainbridge and Beddard applied Bradford's technique to three cats. With regard to the effects of such operations on the amount and concentration of the urine they make the following observations:—

"Making allowance for variations of diet, we find no evidence that the amount and specific gravity of the urine are necessarily modified by either the first or second operation. Only one cat almost invariably passed abundant quantities of dilute urine after the first operation, the others often passed a concentrated urine. . . . It may be concluded, therefore, that the increase in quantity and decrease in concentration of dog's urine after operations on the kidneys is an incidental rather than an essential result."

But even the incidental disclosure of a mechanism may detract in no measure from the importance of the recognition of such mechanism in attempts to interpret the polyuria resulting from disease. In Pearce's experiments which were made on dogs no comments were made on the volume of the urine, since the experiments were designed to check Rose Bradford's observations on the influence of the kidney on nitrogenous metabolism. In the two experiments, however, in which it is possible to compare the outputs of water before and after the reduction in renal substance, it is significant that water additional to the usual allowance was given in the post-operative period, and this increased intake was reflected in an increased output of urine and by a fall in its specific gravity. Pilcher [13] ligated successively the branches of the renal arteries in one cat and one dog and did not observe any change in the output of water. Hermann,[7] on the other hand, recorded an increase in the few of his experiments to which reference was made in the last lecture. The acute effects of ligation of part of the arterial supply to the denervated kidney of the intact dog have, as far as I have been able to determine, not yet been fully investigated. It would appear, then, that an increased output of water following the experimental reduction in the amount of functioning tissue is not invariable in the intact animal. But the important point to realise in so far as the pathology of urinary secretion is concerned, would appear to be the fact of the possible occurrence of such polyuria. Disease may discover mechanisms in the cell which, under experimental conditions, are only brought to light by some peculiar combination of circumstances.

In the experiments on the isolated kidney we saw how the functional removal of approximately half the kidney was followed immediately by an increased flow of urine from the part which was still perfused, an increased flow, moreover, which possessed all the attributes of a pressure diuresis. And we suggested, without being committed to the exact mechanism involved, that each part of the kidney was normally exerting an inhibitory influence over the remainder. Further, it was shown that the functioning part of the kidney was now more susceptible to an externally applied stimulus in the form of a rise in the perfusion pressure. In the whole animal, therefore, it would not be surprising to find that when this second reserve of the kidney was exhausted and all the renal units were receiving the maximum stimulus which under the circumstances could be given them, and yet were unable to cope with the work thrust upon them, there should be a call for external aid in the form of a rise in the general blood pressure.

We must now discuss the means whereby this can be brought about. In 1889 Rose Bradford [5] undertook an investigation into the innervation of the renal blood-vessels, determining amongst other things the origin and course of the vasoconstrictor fibres and the existence and course of the vasodilator fibres. The effects on the kidney volume and on the blood pressure of stimulating the dorsal and lumbar nerves seriatim were investigated. It was found that "stimulation of the anterior roots or of the entire nerve after division of the posterior root" . . . was "followed by contraction of the kidney and a rise of general blood pressure when any nerve from the sixth dorsal to the second lumbar inclusive was the one selected." Although the excitation of all these nerves produced contraction of the kidney and a rise in blood pressure, yet on the whole stimulation of the lower nerves was more efficacious than stimulation of the upper, the greatest contraction of the kidney being caused by stimulation of the eleventh, twelfth, and thirteenth dorsal nerves. Thus the area from which the kidney vessels are supplied is a very extensive one, and, as was pointed out, it was apparently coextensive with that supplying the abdominal vessels. It was now found that when such a nerve as the thirteenth dorsal, which with quick rates of stimulation always gave a renal contraction and a rise of general blood pressure, was excited by means of slow rhythmic break shocks of one per second or even one every two seconds, the kidney underwent marked expansion and no change in blood pressure occurred. "Just as the quick rate of excitation invariably produced contraction of the kidney, so the slow rate produced expansion." "This renal expansion had a short latent period and the rate of expansion was slow, considerably slower than the rate of contraction for the same nerve. Like the contraction effect, however, the expansion was of a persistent character, and generally the kidney remained for a variable time more expanded than it was previously to the stimulation." This true active dilatation of the kidney was only to be obtained by the stimulation of such a comparatively restricted series of nerves as the eleventh, twelfth, and thirteenth dorsal, the same series as that for which the most marked renal vasoconstriction was observed when high rates of stimulation were employed. The presence of these dilator fibres was demonstrated in the splanchnic nerves, and no evidence was obtained which militated against the view that the renal vasodilator nerves reached the kidney by the same path as that followed by the renal vasoconstrictor nerves.

So far, then, the existence of efferent vasodilator as well as vasoconstrictor nerves to the kidney had been clearly demonstrated, the nerves leaving the cord in the anterior roots of the lower thoracic nerves, passing thence to the splanchnic and so to the renal plexus. The reflex phenomena of the renal vessels were next investigated, and it was shown that by reflex excitation, be it from the central end of the sciatic or from the central end of an intercostal nerve, it was more common to obtain contraction than expansion of the kidney, but that expansion was frequently obtained by the excitation of a posterior root of a nerve belonging to what may be called the renal area—i.e., eleventh, twelfth, and thirteenth thoracic. I will, if I may, quote from one of Rose Bradford's papers ([5a]):—

"If a posterior root below the third lumbar nerve be excited, the rise of blood pressure is similar to that seen

on excitation of the great sciatic; if, however, the central end of one of the upper lumbar or lower dorsal posterior roots be excited the rise of blood pressure is far greater in amount and more sudden in its onset; in fact, the effect is quite different to that seen with the lower roots. The anterior roots of these nerves contain, as we have seen, the vasoconstrictor fibres distributed to the vessels of the viscera, and these observations tend to show that these posterior roots also contain special afferent fibres capable of affecting the vasomotor system to a far greater extent than the ordinary afferent fibres seen in sensory nerves. In other words, this great and sudden effect on the blood pressure would tend to show that some posterior roots contain afferent fibres derived probably from the viscera and from the kidney, amongst other viscera. The fact that there are such nerves distributed to the kidney and that the excitation of their central ends is capable of causing a very great effect on the vessels of the body generally, is also a fact that may have some bearing on the production of high tension in certain renal diseases. The other point of interest about these afferent visceral fibres is that, although their excitation causes a rise of blood pressure with general constriction, there is a local dilatation of the kidney—in fact, this is the only method by which, experimentally, any very considerable dilatation of the renal blood-vessels can be produced."

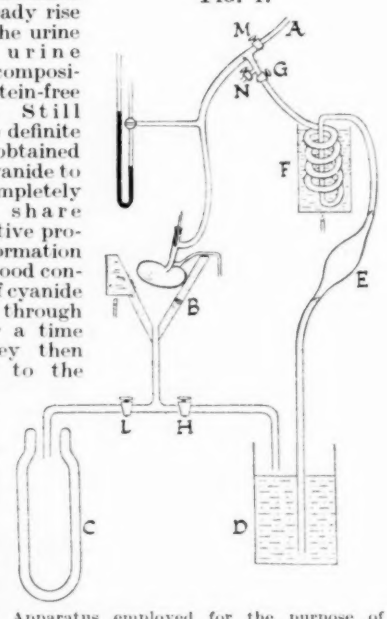
Stimulation, then, of the afferent visceral nerves in the renal area will lead to a reflex active dilatation of the renal vessels and reflex constriction of the vessels of other viscera, occasioning a rise in the general blood pressure.

In the normal animal, however, any rise in general blood pressure is quickly compensated by the bringing into play of the depressor mechanism. A rise in cerebral blood pressure leads, as the cross circulation experiments of Anrep and Starling [1] have clearly shown, to depression of the vasomotor centre and dilatation of the vessels in the splanchnic area. This maintenance of constancy in the arterial blood pressure is one of the most remarkable of physiological facts, any increase in the blood-supply to a particular organ or part of the body being instituted by a redistribution of blood at constant blood pressure. In the normal animal, therefore, the mechanism for causing an increase in the blood flow through the kidney at a constant mean arterial blood pressure is present, and if such reflex dilatation of the renal vessels were exerted to a greater extent on the vasa afferentia of the kidney than on the vasa efferentia an increased glomerular pressure would result. A *sustained* increase in the general arterial pressure could theoretically be initiated in one or more of three ways: firstly, by a general diminution in the capacity of the cardiovascular system produced, for example, by the presence in the blood stream of a substance which caused and maintained an increased degree of contraction of the smaller blood-vessels; secondly, by the continuous stimulation of afferent visceral nerves passing to the vasomotor centre, thus maintaining it in a continued state of increased tone; and, thirdly, by the action of some substance of a chemical nature directly on the vasomotor centre, setting it, so to speak, at a higher tonic register, just as the fever toxins set the thermoregulatory centre to work at a higher body temperature. The mechanism of the production of high blood pressure in man is quite unknown, but in the light of our physiological knowledge of the vital importance of the vasomotor centre in maintaining and controlling the level of the arterial blood pressure in the normal animal, and of our pharmacological knowledge of the manner in which this centre can be influenced by the presence of drugs in the blood stream, it would seem irrational to adopt in explanation of this condition any theory which failed to involve the vasomotor centre as a causative factor in its production. In the high tension found in kidney disease, therefore, our physiological knowledge would predispose us to the view that its original cause was to be found either in a reflex, initiated in the kidney, to the vasomotor centre, or in the circulation of some abnormal substance, or normal substance present in abnormal amount, which had a sustained influence on this centre. In this connexion it would seem advisable to bear in mind the possibility of the vasomotor centre's permanently retaining a functional state originally impressed upon it by nervous or chemical agencies which later cease to function or disappear.

It need scarcely be remarked that mere diminution in the blood flow through the kidney, considered purely as causing mechanically an increase in the peripheral resistance of the vascular system, cannot be entertained as a primary factor in the production of the high tension with which we are concerned.

We must now pass to a brief consideration of the effects of anæmia on the kidney. Temporary asphyxia of the kidney by occlusion of the renal artery was shown by Marshall and Crane [2] to produce on release of the vessel a urine which approached in its percentage composition the blood plasma. Moreover, the urine contained protein, but this quickly disappeared and the composition of the urine soon returned to its state before the artery was occluded. Similar effects can be shown to be produced in the heart-lung-kidney preparation. In the experiment to which I am referring, after obtaining a number of samples of urine from the surviving kidney the artificial respiration was stopped. The heart continued to beat and to maintain a blood pressure of 110 mm. Hg, while the blood in circulation gradually became darker as the heart and kidney used up the oxygen. Towards the end of the asphyxial period and up to the time that the heart failed there was a steady rise of chloride in the urine—i.e., the urine approached in composition the protein-free blood plasma. Still better and more definite results were obtained by the use of cyanide to inhibit or completely eliminate the share taken by oxidative processes in the formation of the urine. Blood containing a trace of cyanide was pumped through the kidney for a time and the kidney then switched back to the heart-lung preparation.

FIG. 1.

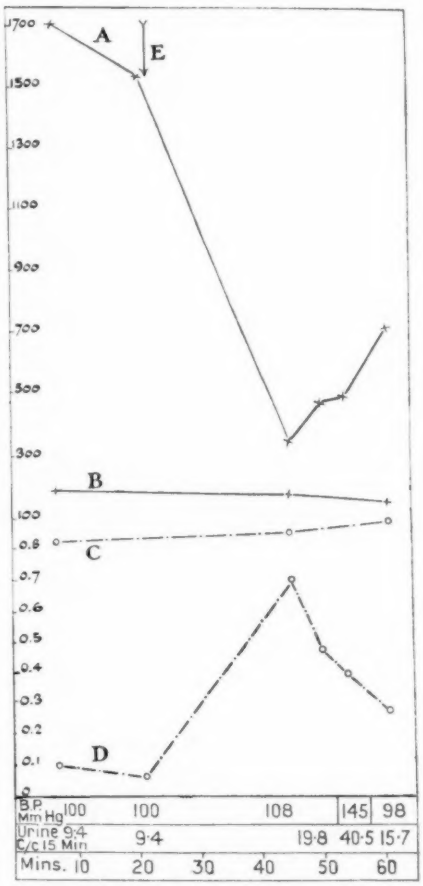


Apparatus employed for the purpose of asphyxiating the kidney suddenly and for a short period of time. For description see text. (E. H. Starling and E. B. Verney. From Proc. Roy. Soc. B., 1925, xcvii.)

The apparatus employed is shown in Fig. 1. The tube A comes from the heart-lung preparation and conducts the blood to the kidney supported in the water-jacketed funnel B. The outflow tube from this funnel passes on the one hand to the Dewar flask C, and on the other to the reservoir D. This reservoir is connected by means of a rubber syringe E and warming coil F to a T-piece in the arterial tube from the heart-lung preparation. Samples of urine are collected and some of the blood of the preparation placed in the reservoir D. To this is added a trace of NaCN, and the syringe, warming coil and tubing are then filled with the mixture as far as the tap G. The blood is being collected from the kidney in the Dewar flask C, the tap H being closed. At a given moment taps M and L are closed, taps G and H opened, and the syringe rhythmically compressed by hand so as to maintain the blood pressure constant at its original level. This is continued for some minutes, when by appropriate turning of the taps already mentioned, the kidney is switched back to its original circulation, and further samples of urine collected for analysis.

The results of one such experiment are plotted in Fig. 2. The temporary approach of the urine in its composition to that of the plasma is graphically represented as well as the speedy recovery which ensues on resuming the natural circulation. In some further experiments performed by Prof. Starling and myself[17] the kidney was perfused by means of a mechanical pump for longer periods of time with cyanided blood, and under these circumstances a pure filtrate of the blood plasma was obtained. The kidney failure was complete, but on reverting to the heart-lung circulation recovery of the organ set in. The kidney cannot be kept for long periods in a state of suspended animation by the use of cyanide. Although during the first ten minutes the filtrate obtained is perfectly free from protein, in the next five or ten minutes a small trace appears, and this amount gradually increases as time goes on. These experiments and those of Marshall and Crane demonstrate how sensitive the kidney is to its contemporary oxygen-supply, and how any interference with this supply speedily leads to failure of the renal units, partial or complete, and to the appearance of protein in the urine. It will be evident that such failure will be accompanied by a retention in the blood of those substances which are normally concentrated during the course of their excretion, and that the degree of this retention in the case of any particular substance will vary directly with the degree to which this substance is normally concentrated by the kidney. In chronic nephritis with polyuria it is the high threshold substances which accumulate in the blood stream.

FIG. 2.



The effects of asphyxia on the composition of the urine secreted by the isolated kidney of the dog. A = urine urea, B = serum urea in mg. per cent., C = serum chloride, D = urine chloride in g. per cent. (as NaCl). At E cyanided blood was pumped through the kidney for 10 mins. (E. H. Starling and E. B. Verney. From Proc. Roy. Soc., B., 1925, xcvii.)

Other experimental facts which have a bearing on the pathology of chronic nephritis will now be briefly mentioned. Firstly, that hypertrophy of the remaining tissue occurs as the result of removing some of the renal substance is well recognised. The hypertrophy, as Sapphir[16] has shown, is accompanied by the enlargement of the existing glomeruli—no new formation of glomeruli and tubules was seen. Secondly, as we saw in the last lecture, when a part of the renal tissue is functionally excluded, the reactiveness of the kidney to the addition of such substances as sodium sulphate and pituitrin to the blood stream is markedly diminished.

In the light of, and as far as possible in terms of the knowledge which has been gained on renal function as the result of physiological and pathological experimentation, it is now proposed to attempt to give a connected picture of the course of the disease of which polyuria forms so striking a symptom. We shall not consider the pathology of the so-called chronic parenchymatous nephritis with its prominent sign of œdema; rather shall we try to trace the course of that type of chronic nephritis which progresses to death without any sign, or one only of the slightest degree, of œdema. We assume the action on the glomerular vasculature of some toxin continuously or discontinuously applied, and leading to a gradual impoverishment in the blood-supply to the renal units. A diminution in the efficiency of the unit as a whole is thus produced. I can find no convincing evidence that in this disease any specific mechanisms within the individual renal unit are functionally impaired to an extent greater than the remaining mechanisms. Fishberg ([5b]) has come to a similar conclusion. I will illustrate my meaning more fully by referring to the actions of two drugs on the kidney. Caffeine, as Dr. Winton and I[19] have shown on the double heart-lung-kidney preparation, causes an increased flow of urine from the isolated kidney. The composition of this urine is, as far as we have been able to determine, the same as that of the urine produced by the control kidney when the perfusion pressure of this kidney is raised to such a degree that the diuresis so produced is the same as that occasioned by the action of caffeine on the other kidney. Caffeine diuresis, therefore, is a "pressure" diuresis, the individual units in the kidney being simply stimulated to do more work. Phlorhizin, on the other hand, picks out one particular mechanism, the sugar excretory mechanism, in the unit, and the compositions of the urine from each kidney at the same rate of urine flow would in consequence be different (De Boer and Verney).[3] There seems to be no evidence that in chronic nephritis the response of the individual units are affected in any way other than that resulting from a gradual or rapid fall in the efficiency of the whole unit. In the advanced state of the disease the units are in all probability in very different states of efficiency ranging perhaps from normal to zero. In the normal kidney the efficiency of the units composing it may be considered to be high and uniform, in the chronically inflamed kidney low and variable. We may *speculate*, then, somewhat as follows:—

The first effect of the hypothetical toxin on the normal kidney will be to lead to a reduction in the periods of quiescence of some or all of the units of which it is composed. The first reserves of the kidney have been requisitioned. Later the work thrown on the kidney during the day is unable to be completely dealt with, and the composition of the blood is brought back to its physiological optimum by an encroachment on the normal period of nocturnal rest. An increased urine flow during the day and during the night gradually becomes detectable, and is the expression of the increasing failure of the individual units of the kidney. The complete failure of some leads to the appearance of albumin in the urine. Their death with replacement fibrosis leads to a removal of that inhibition on the remainder which the work I described in the last lecture on the isolated kidney led us to postulate. The remaining units are now in a position to receive a greater pressure stimulus and they react to this increased stimulus, as we have seen from the experiments of Rose Bradford and from those on the

isolated kidney, by secreting a more copious urine and one which approaches towards the plasma in its composition. Doubtless a work hypertrophy of these units also occurs, but such is insufficient to neutralise the loss of efficiency due to the gradual encroachment of the disease. No difficulty is being experienced, as we have seen in the experiments on the isolated kidney, in the excretion of chloride, but there results an increasing retention of urea and of those substances secreted by a similar mechanism. Eventually the *intrinsically* developed pressure stimulus is itself insufficient to bring about a sufficiently great response by those units which remain in activity. They are working at their maximum under the existing circulatory conditions, and a call is initiated for a further stimulus. This is responded to by an increase in the general blood pressure, and we have already considered the physiological mechanisms by which such a rise can be produced. Whether one of these known mechanisms is involved or not in the production of the high blood pressure of this disease, it is impossible to say in the present state of knowledge. With the death of still further units the work of the remainder can only be increased by a still further rise in blood pressure. The polyuria, then, will be persistent and, coincidently with the falling efficiency of those units which remain to function, its degree must become accentuated if any balance is to be maintained between the production and excretion of bodies such as urea and those eliminated by a similar mechanism. The balance becomes in time too negative to be compatible with life. Such a hypothetical picture of the gradual production and increasing intensity of the polyuria of chronic nephritis is based almost exclusively on physiological mechanisms in so far as they are at present known to exist in manifest or latent form. But the manner in which such mechanisms are correlated and integrated in the struggle to preserve the composition of the body fluids at their optimum is entirely unknown.

In concluding this lecture emphasis may be laid on what may be conceived to be the two essential functional changes responsible for the polyuria of chronic nephritis—viz., an increase in the pressure stimulus to secretion accompanied by a decrease in the efficiency of the kidney as a whole. That is to say, the composition of the urine from a normal kidney supplied with the same blood and secreting at the same rate, would exhibit a far greater recession from that of the plasma than the composition of the urine from a kidney which is the seat of this disease. And that the efficiencies, in this sense, of the individual units of the kidney are also diminished in this condition to varying degrees, would seem extremely probable.

Before I close I should like to thank you, Sir, and the College most warmly for the great honour you have done me in asking me to give these lectures, and although I have not faithfully adhered to the request of the Founder that the lecture should be read "between Michaelmas and Easter, on three days together, both forenoon and afternoon, on some dead body if possibly it can be procured, which shall then and there be dissected for the diseases treated of, and shall afterwards be buried," I hope that the observations which have been brought forward are not entirely irrelevant to the spirit in which this lectureship was founded.

REFERENCES.

1. Anrep, G. v., and Starling, E. H.: Proc. Roy. Soc. B., 1925, xcvii., 463.
2. Bainbridge, F. A., and Beddard, A. P.: Ibid., 1907, lxxix., 75.
3. Boer, de, S., and Verney, E. B.: Jour. Physiol., 1924, lviii., 433.
4. Bradford, J. R.: Ibid., 1899, xxiii., 415.
5. Same author: Ibid., 1889, x., 358.
5a. Same author: THE LANCET, 1898, i., 765.
5b. Fishberg, A. M.: Arch. Internal Med., 1926, xxxviii., 259.
5c. Hart, P. d'A.: Personal communication.
6. Hedinger, M., and Schlayer, C.: Deut. Arch. f. klin. Med., 1914, cxiv., 120.

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THE ADMINISTRATION OF INSULIN IN SUSPENSION.

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DELIBERATION over the inadequate treatment of one disease occasionally leads to the benefit of patients suffering from another.

Many years ago the tortures suffered by children in whom pericardial adhesion had led to enormous hypertrophy of the heart made me seek some means of preventing the development of this condition. I thought that perhaps a non-absorbable oil such as liquid paraffin, if introduced during the period of effusion, might prevent the adhesion of the visceral and parietal layers of the pericardium. I began by introducing liquid paraffin into the pleural cavities of guinea-pigs and found that this was an efficient method of preventing adhesion when inflammation was produced by injection of aleuron. This has led to the use of liquid paraffin in pleural effusion and has benefited many patients suffering from that complaint, but has not been used to any extent in the much less common disease, pericardial effusion.

The origin of the work which I am recording in this paper, too, was indirect. In the treatment of diabetes insipidus the injection of five units of some extracts of pituitary gland will control the flow of urine for about four hours. If ten units be given the control may extend to six hours, but a contraction of the bowel is sometimes caused in susceptible subjects. Any further increase in the dose does not appreciably increase the length of time that the diuresis is controlled.

The Problem of Discontinuous Absorption.

Recently I have been supplied with extracts of pituitary gland which contain some quantity of antidiuretic material but very little vasopressin and oxytocin. Their injection does not lead to discomfort, but as they do not contain the substance which causes constriction of the blood-vessels, their absorption is rapid and, consequently, their action is not so prolonged as if they were slowly absorbed. It occurred to me that by making an emulsion I might delay absorption and control the diuresis for 24 hours by a single injection. The antidiuretic substance in pituitary extract might be difficult to prepare as a powder and therefore it seemed wise to transfer the observations to some other substance for a time and return to the treatment of diabetes insipidus at a later date.

I began experiments upon delay in the absorption of insulin and asked a manufacturer to supply me with the drug suspended in oil, thinking that by

PROF. E. B. VERNEY: REFERENCES.

(*Continued from previous column.*)

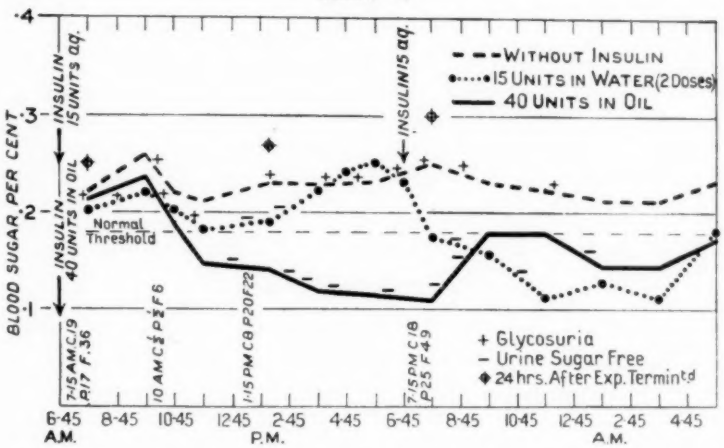
7. Hermann, M.: Sitzungsber. d. k. Akad. d. Wiss. z. Wien (Math.-Naturwiss. Classe), 1862, xlv., 317.
8. Löhlein: Über die entzünd. Veränderungen der Glomeruli bei mensch. Nieren u. ihre Bedeutung f. die Nephritis, Leipzig, 1906. (Cited from Volhard and Fahr, q.v.).
9. Marshall, E. K., and Crane, M. M.: Amer. Jour. Physiol., 1923, lxiv., 387.
10. Mosenthal, H. O.: Arch. Internal Med., 1918, xxii., 770.
11. Osler, W., and McCrae, T.: Principles and Practice of Medicine, New York and London, 9th ed., 1920, p. 702.
12. Pearce, R. M.: Jour. Exp. Med., 1908, x., 632.
13. Pilcher, J. D.: Jour. Biol. Chem., 1913, xiv., 389.
14. Quincke, H.: Arch. f. exp. Path. u. Pharm., 1893, xxxii., 211.
15. Richards, A. N., and Schmidt, C. F.: Amer. Jour. Physiol., 1924, lxxi., 178; Wearn, J. T., and Richards, A. N.: Ibid., p. 209.
16. Sapphir, O.: Amer. Jour. Path., 1927, iii., 329.
17. Starling and Verney: Proc. Roy. Soc. B., 1925, xcvii., 321.
18. Traut, H. F.: Contributions to Embryology, Washington, 1923, vol. xv.
19. Verney and Winton, F. R.: Unpublished Observations.
20. Volhard, F., and Fahr, Th.: Die Bright'sche Nierenkrankheit., Berlin.

administering it in suspension its action could be made less intense and more prolonged. At first sight it seemed doubtful whether much would be gained, because it was generally accepted that the best way of giving insulin was to inject, shortly before a meal, the amount needed to katabolise the carbohydrates in that meal. Upon further consideration, however, one is forced to the conclusion that insulin is liberated continuously in the normal body, a larger supply being made available when the sugar in the blood rises above a certain level. The evidence for this conclusion lies in the following facts:—

1. That neoplasm of the islands of Langerhans leads to death from hypoglycæmia.
2. That persistent hypoglycæmia may occur in individuals who have never received insulin and who, upon exploratory laparotomy do not present any enlargement of the pancreas. These die if they are not fed with carbohydrate at short intervals.
3. Cases of persistent hypoglycæmia following the administration of insulin may occur. I have seen the sugar in the blood fall to 0·03 per cent. although insulin had not been given during the previous ten days. One imagines that in these cases the pancreas continues to secrete insulin slowly whilst there is some diminution in the activity of glycolytic ferment.
4. During sleep carbohydrate must be burnt, some from the glycogen stored in the liver and tissues, and some from the protein which is broken down, and for this purpose insulin must be supplied. In the normal individual the concentration of sugar in the blood during the night does not rise sufficiently high to stimulate the production of insulin. If carbohydrate katabolism were to cease during the night, ketosis would develop in some people.

If the pancreas were only to secrete insulin when the sugar in the blood rose above 0·16 per cent., then it would be difficult to imagine how hypoglycæmia could be produced in any other way than by the direct injection of insulin.

CHART 1.



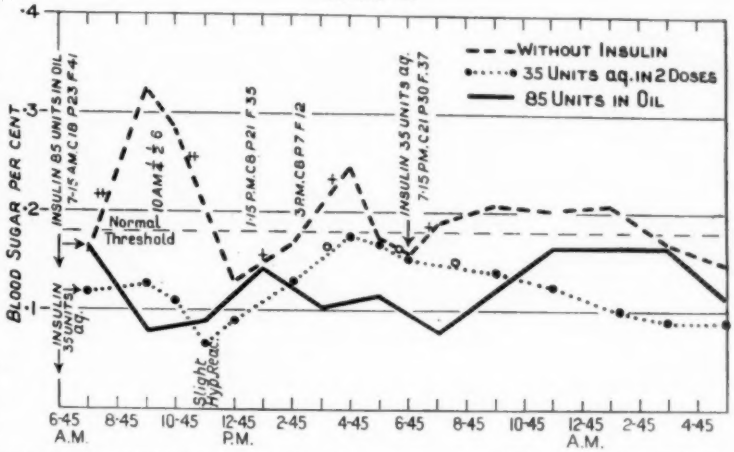
Points in Practice.

Medium of Suspension.—At first it seemed to me probable that an emulsion might be made with the help of lecithin. This indeed proved possible, but the method was soon abandoned because the preparation was not stable.

I then asked for suspensions of pure dry insulin in oil, and Dr. S. W. S. Underhill was so good as to make some experiments in this direction. He found that if insulin were ground up with oils and then centrifugalised, some oils kept the insulin in suspension whilst others allowed it to settle. Probably this depends upon the specific gravity of the oil and also its viscosity and the fine state of division of the insulin.

Arachis oil suspended 60 units per cubic centimetre and possessed many properties which recommended it for use, but unfortunately a certain percentage of patients complained of pain after its injection.

CHART 2.



Castor oil was then tried. This oil can suspend more than 100 units per c.cm. of the insulin prepared by British Drug Houses, Ltd. The specific gravity of this oil is about 0·964, against arachis oil 0·918. I found that castor oil did not give pain. No doubt a better medium will be used shortly but for the present it suffices; the suspension appears to be stable and the insulin does not deteriorate rapidly.

Method of Injection.—Obviously a viscid oil must be injected in a different manner to an aqueous solution. The points which should be observed are: (1) The oil should be warmed before injection, in order to reduce its viscosity (in very cold weather). (2) A thick needle must be used to draw it into the syringe. (3) A needle less fine than that used for aqueous solutions must be chosen for the actual injection; it should be short. (4) A screw-down syringe may be used if the muscles of the thumb of the injector be weak. (5) Lastly, but most important of all, the injection must *not* be intramuscular but subcutaneous. Experience has shown that the least discomfort follows injection under the skin of the abdomen, the injection being given before the patient rises in the morning.

Methods of determining which concentration of insulin in suspension is the most satisfactory.—In my opinion there is a tendency to make all patients conform to the same rules, a procedure which saves work but prevents attainment of the best results. For instance, many advise that the injection of insulin in solution be given 20 minutes before a meal; whereas investigation has taught me that some patients derive more benefit by receiving the insulin 5 minutes, others up to 90 minutes, before the meal. It is unreasonable to expect that all individuals will absorb oleum ricini given subcutaneously at the same rate, or that they will need the same flow of insulin into their tissues. I have therefore made observations with suspensions containing 100, 50, and 25 units per c.cm. When opportunity offers, it is undoubtedly wise to

take samples of blood at short intervals and estimate the concentration of sugar in them. If the fall be rapid after the injection, then it would be wise to diminish the concentration of insulin in the oil and vice versa. If there be no opportunity of estimating the sugar in the blood, one of the two following methods may be used:—

1. After an injection of a suspension containing 100 units of insulin per c.cm., urine may be passed every two hours, and it is noted how long it takes for sugar to be excreted in recognisable quantity. This experiment should be continued for two or three days, and then the same dose of insulin should be injected in a larger volume of oil, and once more observations should be made to determine the period during which glycosuria is controlled. By trying different doses and different concentrations, glycosuria may be abolished completely, provided the diet is not greatly excessive and the patient is not completely resistant to insulin.

2. The urine during the 24 hours is collected, mixed, and measured, and the percentage of sugar in it estimated. This is repeated for three days, then the same dose of insulin, but in a different concentration, is given and observations are made as to whether the sugar excreted is increased or diminished. Usually this gives a clue of how it can be abolished completely.

Illustrative Cases.

Chart 1 illustrates the effect of insulin upon a patient suffering from moderate diabetes mellitus. His diet consisted of: Breakfast, carbohydrate 19 g., protein 17 g., fat 36 g.; lunch at 10 A.M., consisting of carbohydrate 0·5 g., protein 0·5 g., fat 6 g.; dinner at 1.15 P.M., carbohydrate 8 g., protein 20 g., fat 22 g.; supper at 7.15, carbohydrate 18 g., protein 25 g., fat 49 g. This diet was arranged for two doses of aqueous solution of insulin—one was given at 6.45 A.M., and the second at 6.45 P.M. The dotted line shows the rise and fall of the sugar in the blood on that diet and doses of insulin. On the next day 40 units of insulin in oil were administered at 6.45, and the black continuous line shows the rise and fall of the concentration of sugar following that. In all probability the line would have been somewhat flatter if the midday meal had contained more carbohydrate and the evening meal rather less, but the comparison was made with the diet arranged from best results with the two injections. The third line shows the sugar in the blood when insulin has not been given, but apparently the effect of insulin is carried over for more than 24 hours and, on making estimations on the second day of the cessation of insulin, sugar in the blood is found to rise to 0·3 per cent. at 7.30 P.M.

CHART 3.

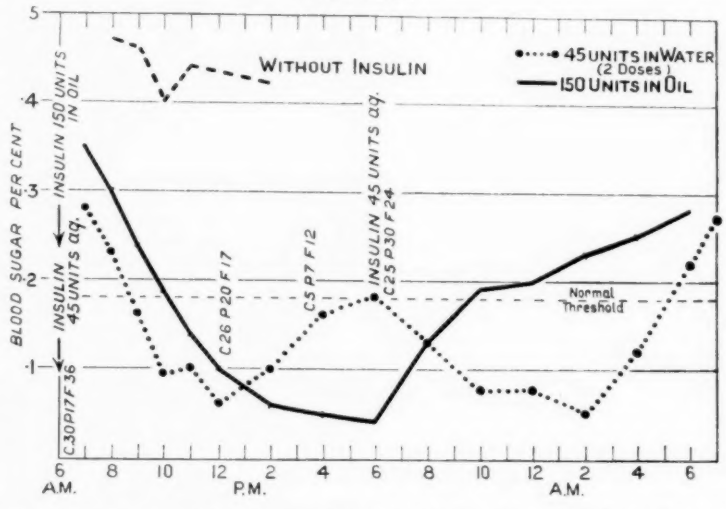


Chart 2.—A patient suffering from somewhat more severe diabetes mellitus. The diet consisted of: Breakfast, carbohydrate 18 g., protein 23 g., fat 41 g.; morning lunch, carbohydrate 0·25 g., protein 0·5 g., fat 6 g.; at 1.15 P.M., carbohydrate 8 g., protein 21 g., fat 35 g.; at 3 P.M., carbohydrate 8 g., protein 7 g., fat 12 g.; at 7.15, carbohydrate 21 g., protein 30 g., fat 37 g.

After the morning dose of 35 units of insulin in solution, the sugar in the blood fell at 11 o'clock sufficiently low to produce symptoms of hypoglycæmia. Towards 5 P.M. the sugar in the blood approached the threshold, started falling, fell and continued to fall after the evening dose at 6.45 of 35 units of insulin. When observations were made upon the action of insulin in oil, the sugar in the blood started considerably higher than on the day chosen for observation with aqueous solution of insulin. The sugar in the blood fell well below 0·1 per cent., but not sufficiently low to give rise to symptoms of hypoglycæmia. Sugar in the blood remained below 0·15 per cent. until 11 P.M., when it rose to 1·7 per cent. I have little doubt that here, too, if some of the carbohydrate given at the evening meal had been transferred to lunch or tea, the sugar in the blood would not have risen so high. The third curve shows the rise and fall of the sugar in the blood when insulin was withheld. The sign O indicates that sugar was not found in the urine whilst the sign + indicates the presence of sugar.

Chart 3 was prepared from observations on a very severe case of diabetes mellitus, so severe that the omission of one dose of insulin led to symptoms of ketosis, whilst the sugar in the blood rose to 0·45 per cent. The patient's diet, however, was quite liberal. Breakfast consisted of carbohydrate 30 g., protein 17 g., fat 36 g.; the midday meal, carbohydrate 26 g., protein 20 g., fat, 17 g.; tea, carbohydrate 5 g., protein 7 g., fat 12 g.; and the evening meal, carbohydrate 25 g., protein 30 g., fat 24 g.

Examination of this chart illustrates very definitely that it is unwise to treat all cases in the same way. The patient was able to absorb insulin in suspension at too rapid a rate when injected in a concentration of 90 units per c.cm.; the effect was too transient, and insulin did not appear to be available for the metabolism of the evening meal. Although the dose of insulin was greater when the single dose was given than when the two aqueous doses were injected, nevertheless 50 g. more sugar were excreted. I concluded that it would be wise to reduce the concentration of the suspension. When the same dose of insulin was given in a suspension of 50 units per c.cm. 30 g. less sugar was excreted than when the two aqueous injections were given—that is to say, 80 g. more carbohydrate was utilised by reducing the concentration of the suspension.

The advantage I claim for the suspension of insulin is, that it will lead to a greater number of recoveries from diabetes mellitus. In my experience cases of recovery have been confined to those who, month after month, have kept the concentration of sugar in their blood continuously below 0·15 per cent. The prolonged action of the suspension will make this much less difficult. In all probability a number of drugs, in addition to insulin and the antidiuretic substance from the pituitary gland, may with advantage be administered in suspension.

It is with the greatest of pleasure that I express my thanks to my first assistant at the London Hospital,

Dr. F. B. Byrom, who carried out numberless estimations and sacrificed many hours of sleep in order that the records of cases might be complete. Dr. J. L. F. Steele and Miss R. M. Simmonds, the dietitian to the hospital, rendered invaluable assistance.

PULMONARY NEOPLASMS.

A REPORT OF TWENTY-SIX CASES.

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THE growing literature on the subject of intrathoracic tumours has shown from all sides an increased incidence of this condition in recent years. Though this increase is considered by some to be more apparent than real and is attributed, for example, by Fried [17] to better diagnosis, to a larger attendance at hospital, and to "increased human longevity," yet the careful and extensive reports of post-mortem statistics from many German and other authors have proved almost beyond doubt that a true increase has actually taken place. Statistics from the post-mortem records of St. Mary's Hospital are at present being collected and are shortly to be published. When it is realised that pulmonary neoplasm is found in approximately 7 per cent. of all autopsies on patients dead from carcinoma (various figures being 9·7 per cent. Wahl,[35] 10·7 per cent. Ferenczy and Matolcsy,[14] 5 per cent. Lubarsch,[25] 8·9 per cent. Biberfeld [6]) and ranks next in frequency only to carcinoma of the stomach, breast, uterus, and œsophagus (Lighty, Wright, and Baumgartner,[24] Gruber [19]) its importance can hardly be over-estimated. Since, furthermore, the percentage of early correct diagnoses is not generally greater than 33 per cent. (Sehrt [30] 4 per cent., Ferenczy [14] 25 per cent.), a further report of even a few cases only may be of some value.

The 26 cases here described have all been in the wards of St. Mary's Hospital at some period during the last six years (1922–28), and all have been examined post mortem. Twenty of them were in the Medical Unit wards (under Prof. F. Langmead); for permission to examine the notes of the remaining six patients I am indebted to Sir John Broadbent, under whose care they were.

The post-mortem findings confirm the now well-recognised fact that the overwhelming majority of intrathoracic neoplasms—often wrongly called "mediastinal tumours"—are in fact not mediastinal in origin—i.e., sarcomatous—but are of true carcinomatous nature. Of these 26 cases, for the histological examination of which my thanks are due to Dr. W. Newcomb, 21 are of the "oat-celled" type, three are composed of mixed polygonal and columnar cells, and two of squamous cells. They are thus, according to the views of the majority of workers on this subject, all carcinomata, the very common "oat-celled" type being considered either as a true bronchial mucosa tumour (Barnard,[4] Aschoff [2]), or as a growth of the alveolar lung epithelium itself.

Primary lung sarcoma and true mediastinal lymphosarcoma are undoubtedly rare. Staehelin [34] finds intrathoracic neoplasms to be almost all bronchial carcinomata. Barnard,[4] Fishberg,[16] Ferenczy,[14] Brandt,[7] Duguid,[10] Shennan,[32] and many others agree, and Sonnenfeld [33] saw only one case of sarcoma and affirmed that at least 95 per cent. of primary thoracic new growths are in fact bronchial carcinomata. Among 30 cases examined by Dr. Newcomb at St. Mary's Hospital only one was a fibrosarcoma of lung, one a true lymphosarcoma of the mediastinum, and one a teratoblastoma; the remaining 27 were carcinomata, 21 being of the "typical oat-celled" type, four of mainly polygonal-cell structure, and two of squamous epithelium.

Sex, Age, and Localisation.

Of the 26 patients here described 20 were men and only 6 were women. This shows a male preponderance of more than 3 to 1, which is even greater than has been found in many other series. Ferenczy [14] quotes 16 writers who all found a marked preponderance of male over female. Ewing [13] gives 71·9 per cent. as the percentage of men affected in 100 cases; Kikuth [23] and Dynkin [11] and Sachs [27] place the rates at 1·9 to 1 and 1·8 to 1. Ferenczy's own cases showed almost a 3 to 1 relationship; Rubenstone [26] found 8 men in 11 cases and Shennan [32] 27 in 31.

The average age was 50 years, the youngest being 27 and the oldest 79; this agrees with statistics of German writers who find the maximal incidence of these tumours between the ages of 50 and 60.

Sixteen—or 64 per cent.—originated, as far as could be determined, on the right side, and of these growths nine appeared primarily to have affected the upper lobe and seven involved either the whole lung or were mainly basal. An excessive incidence of right over left lung has been frequently noticed, Seyfarth [31] finding a ratio of 2 to 1. Holzers,[20] Briese's,[8] and Wolf's [36] figures agree, but Kikuth [23] and Marchesan found no appreciable difference. Many suggestions have been made to account for this increased liability of males to pulmonary carcinoma, particularly in the right lung, and any theory of ætiology must in some measure explain these facts. Some have thought that the more frequent respiratory "insults" that man, as compared to woman, must meet in his work, may account for this difference; road dust, tobacco, tar particles, cobalt, and arsenic in the air are some of the possible causal factors put forward. Duguid found that outdoor workers in Manchester seemed more liable to these tumours than those who worked in more sheltered conditions; Hudson [21] found a high incidence in grooms and stablemen. Shennan,[32] however, found nothing suggestive in the previous occupations of his patients, nor could Sehrt [30] connect these growths with any particular profession. Seyfarth's [31] patients were mainly labourers and land-workers, and 75 per cent. of Ferenczy's patients were also labourers, 43 per cent. of whom had had work in which the respiratory organs tended especially to be affected. Frommel [18] in France also noted that 29 of his 41 patients had been especially liable in their professions to inhalation of road dust. It seems that in recent years some new agent has appeared or increased in the air, which in some way makes the bronchial mucosa more liable to new growth formation.

The suggestion of Schwyter [29] (who found congenital malformation of the lung tissue in the neighbourhood of the growth in five cases out of eight) that developmental errors may be a cause of pulmonary carcinoma, remains unconfirmed. There is, however, some evidence to show that simple chronic irritation, as, for example, by chronic bronchitis, is an especial predisposing cause; influenza has been particularly blamed in this respect (Feyrter [15]) and tuberculosis has by others been considered as "the chief ætiological factor" (Ewing [13]) and "the forerunner" (Frommel [18]). The incidence of such conditions, however, does not appear to be higher as a whole in patients dying of pulmonary cancer than in those dying of other non-respiratory disease, and both chronic bronchitis and old or active tuberculosis are clearly not uncommon coincident findings in a large proportion of all post mortems. In these 26 cases a very definite history of somewhat severe previous respiratory affections was found in 13—i.e., 50 per cent., made up of influenza (6, including one patient who had also had pneumonia), chronic bronchitis (4), tuberculosis (2), pneumonia (2). Two of these had also suffered from asthmatic attacks. This is a somewhat high incidence and may possibly have some ætiological significance, though not to the same extent as was apparently the case in Berblinger's [5] series, or those of Feyrter or Frommel. In 12 of these patients it is possible to presume some particular liability to respiratory irritation, as they had been respectively: painters (4), engineers (2), dustmen (1), motor drivers (2), carpenter (1), brass-finisher (1), and coal-labourer (1). There was no case

among stablemen as found by Hudson [21] and O'Donnell, nor a special preponderance among outdoor workers. Four patients only gave a history of excessive tobacco-smoking, and in no case was there any suggestive feature in the family history.

Course, Symptoms, and Signs.

The course of bronchial carcinoma has been described as slow and gradual, and this may well be true, since it is rare for patients to come under observation until the growth is well advanced. At actual total duration from the commencement of the growth itself. Fried [17] emphasises the slow growth of these tumours and considers this to be one reason why metastases are so common, but though there is doubtless a relatively long symptomless latent course, it is difficult to believe that the average total duration can be more than two years.

Early diagnosis of pulmonary carcinoma is obviously not of the same hopeful importance as it is, for example, in the case of gastric or mammary cancer, though Sauerbruck [28] Edwards,[12] and Lilianthal have

TABLE SHOWING THE CHIEF CLINICAL FEATURES AND PATHOLOGICAL FINDINGS IN 26 CASES OF PRIMARY NEW GROWTH OF LUNG.

Case.	Sex.	Age.	Occupation.	Previous history of respiratory disease.	Onset (first symptoms).	Hæmoptysis.	Effusion.	Length of life from onset of symptoms in months.	Type of carcinoma.	Situation of growth (probable origin).
1	M.	55	Taxi-driver	Nil	Pain→dyspnœa	None	Purulent	4		R. lower lobe
2	M.	65	Pensioner	Nil	Dyspnœa→cough	Early	None	12½		R. (? upper) lobe
3	F.	40	Housework	Nil	Pain→dyspnœa	Present	Hæmor.	17	Oat-celled	L. lung (entire)
4	M.	32	Grocer	Nil	Aphonia→dyspnœa	None	None	8		L. lung (hilum)
5	M.	51	Salesman	Cough (10 years)	Pain→cough	Early and continued	„	12	Polyg. and col.-celled	L. lung (upper)
6	F.	59	Saleswoman	"Always chest trouble."	Pain→cough	None	„	—		R. lung (root)
7	M.	40	Postman	Nil	As "bronchitis"	Severe	Hæmor.	6		R. lung (root)
8	M.	46	Painter	Influenza (frequent)	Aphonia→cough	None	Bilateral	3	Oat-celled	R. and L. root
9	M.	46	Clerical (G.P.O.)	Nil	Bronchitis→"swelling of neck"	Late	Present	6		R. (? upper) lobe
10	M.	43	Engineer	Influenza, phthisis, bronchitis	Stridor→dysphagia	Present	None	5	Polyg. and col.-celled	R. lung (? upper lobe origin)
11	M.	57	Brass-finisher	Bronchitis (6 years)	Dyspepsia→dysphagia	„	„	3		R. lung (lower)
12	F.	54	Housework	Influenza	Dyspnœa	None	Hæmor.	15		R. lung
13	M.	63	Electrical engineer	Phthisis	Œdema of arm→cough	Early	None	4	Oat-celled	R. upper lobe
14	M.	48	Motor-driver	Nil	Cough	„	Present	6		L. lung
15	M.	58	Painter	Nil	Pain→cough	None	„	1½	Polyg.-celled	L. lung
16	M.	79	—	Nil	Dyspnœa→dysphagia	„	Hæmor.	4		L. lung
17	M.	49	Carpenter	Influenza	Pain→dyspnœa	Present	None	12		L. lung
18	F.	60	—	Asthma, cough (3 years)	Pain→dyspnœa	None	Present	8		R. lung (root)
19	M.	60	Painter	Influenza, bronchitis	"Bronchitis"→pain	„	Hæmor.	4		R. lung (upper)
20	M.	35	Dustman	Pneumonia, influenza	Cough→"swelling of neck"	„	None	3½	Oat-celled	R. lower lobe
21	F.	45	Housework	Nil	No symptoms	„	„	—		L. lung
22	F.	39	Housework	Nil	Œdema of face→dyspnœa	„	Pseudo-chylous	4		R. lower lobe
23	M.	27	Coal-labourer	Nil	Pain→"bronchitis"	Early and continued	Present	6		R. lower lobe
24	M.	60	Publican	"Chronic" cough	Cough→hemiplegia	None	None	7	Squamous-celled	L. lung
25	M.	47	Painter	Pneumonia	Vomiting→"bronchitis"	Present	„	4	Oat-celled	R. upper lobe
26	M.	44	Railway guard	Nil	Pain→coma	None	„	6	Squamous-celled	R. lower lobe

Hæmor., hæmorrhagic. Polyg., polygonal; col., columnar.

Special Features.—CASE 5: Old tuberculosis both lungs (extensive). 6: Death from pulmonary embolism. 8: Origin probably on right side. 10 and 11: Death from profuse hæmoptysis. 12: Collapse and death after aspiration of chest. 14: Bronchiectasis, gangrene, empyema, septicæmia. 16: Pericarditis and heart failure. 21: Accidentally found at autopsy; death from other causes. 23: Pericarditis and heart failure. 24: Secondary deposit in right cerebral cortex. 25: Diagnosed "aneurysm." 26: Secondary deposit in left cerebral cortex.

first the condition causes few symptoms and there is no tendency to cachexia, loss of weight, or anæmia; in our patients the strikingly good general condition was noticeable until the late and final stages of the disease, and in several instances heavy work was continued until within a few weeks of death. When once it has made itself felt, however, bronchial carcinoma takes a rapid course, and the average length of life in these patients from the first definite symptom was almost exactly six and a half months. The shortest duration was one and a half, the longest 17 months. Sonnenfeld [33] found a course—dating from the first symptom—of from three months to three years, but no definite data exist as to the discussed the advantage of thoracotomy and if possible lobectomy early in the disease. From a prognostic point of view, however, it is a vital consideration. A few features only will be here considered. The early symptoms of the condition frequently resemble pulmonary tuberculosis, and it is often diagnosed as such, particularly by X ray evidence (Uspensky [37]). The onset, however, appears often to be with pain, which is not very common in tuberculosis. Among these 25 patients (one, in whom a small symptomless growth was found accidentally at autopsy, is omitted) nine, or 36 per cent., complained at first of pain only; in five cases this preceded any other disturbance by many weeks and

was of a dull, aching character, spreading to the shoulder-blade of the affected side and in two cases down the arm. This is unlike tuberculosis and is very easily mistaken for fibrositis or "neuralgia." It is probably due to pleurisy over the growth, and in a few cases to nerve-pressure with referred pain via the phrenic nerve to the shoulder. Five of these eight patients—or 62 per cent.—either at once or later developed a pleural effusion, so that pleural pain may well account for the majority. In only four cases was a rub heard. Many other cases began as "influenza" or "bronchitis," and a strikingly frequent mode of onset was an acute attack of illness with cough which was invariably diagnosed as "influenza" or "bronchitis"; this kept the patient to his bed for a short time 7 to 21 days—and was followed by a return to work for a few weeks, then a "recrudescence" of the original "influenza," and thenceforth a steady and rapidly progressive course until death. Six of these cases showed exactly this history, and the original acute attack again appears to be due to the first affection of the pleura as the growth spreads outwards, though in no case was it quite typical of an ordinary simple pleurisy. Three patients complained of dyspnœa from pressure on a bronchus as their first symptom (two with cough), and seven suffered from the effects of pressure or other structures—i.e., two from hoarseness and loss of voice (recurrent laryngeal nerve), two from dysphagia (œsophagus), one from stridor (trachea), and two from œdema of the arm or face (large veins). No clear prognostic import could, however, be deduced from the mode of onset in these patients, though those whose illness began with "bronchitis" lived on an average three months longer than those in whom it started with primary pressure symptoms. In no case was hæmoptysis the earliest symptom, as is considered to be frequent by Sonnenfeld (50 per cent.), and indeed the so-called typical red-currant jelly sputum appeared to be actually rare in this condition (see also Abraham [1]). Of these patients, 12—or 48 per cent.—showed during the disease either blood-streaked sputum or a severe hæmoptysis; in five it was an early event, in two it was the immediate cause of death. Cough and dyspnœa were both absent in one patient only, who complained of some pain and dysphagia, was treated by gastrostomy, and died suddenly from a profuse hæmoptysis. The rapid progress of the dyspnœa in the later stages of the disease was very typical, and indeed at this time the diagnosis could often be made at sight. The swollen, congested face and arms, the constant restlessness, and anxious, worried expression formed a characteristic picture.

The physical signs were most variable. In 12 of these patients they were those of effusion; in six the effusion was present on first examination, and in five it developed later in the disease. One patient was operated upon for empyema, and in five cases the fluid was hæmorrhagic. The presence or absence of an effusion did not appear, however, to exert any influence on the duration of the disease, but since it was present in 48 per cent. of these patients an otherwise unexplained effusion in an elderly patient must always arouse suspicions of a growth of the lung. Stachelin [24] found that one-third of his patients already had a pleural effusion when they first came to a doctor. The position of the heart's apex-beat is in such cases often misleading, and indeed in all cases of pulmonary carcinoma appears to be an unreliable guide. In these 25 patients the apex-beat in five was displaced towards the side of the growth, in ten it was displaced towards the healthy side, and in ten no appreciable change was found. Abraham [1] also noted that the displacement of viscera towards the affected side did not exclude growth, and in two patients in this series in which an actual effusion was present such retraction was noticed. Marked flattening of the chest was noticed in three patients only, but impaired movement on respiration was found in sixteen and dullness on percussion in all, either early or late. Bulging of the chest wall occurred in four and an external growth was seen in three. The auscultatory signs varied with the stage of the growth and with the presence or absence of associated infection or effusion. Five patients had the typical signs of a cavity, but the commonest findings were weak or absent breath-sounds with a few coarse râles and slightly diminished vocal resonance. Clearly there can be no constant group of signs typical of pulmonary new growth. Enlargement of veins of the neck or over the thorax, for example, was only noted as an early sign in five patients (or 20 per cent.) and palpable enlarged glands in the neck or axilla occurred only in eight (or 31 per cent.) during the whole course of the disease.

Diagnosis.

Early diagnosis must depend largely upon X rays. The sputum was in no case sufficiently characteristic, and in only three patients did examination of the pleural fluid give definite assistance by showing the large endothelial cells said to be typical of these growths. The physical signs alone were seldom sufficient in themselves to establish an early diagnosis. Fishberg [16] considers that the examination is incomplete unless, besides X rays and lipiodal injection, bronchoscopy with removal of a portion of tissue has also been carried out. When fluid is present X rays alone are especially untrustworthy and can seldom give definite indication of the cause of the effusion. According to Kirklin [22] the three radiological characteristics of early malignant disease are density of the hilum, atelectasis, and bronchiectasis.

The most frequent sources of difficulty in diagnosis in this series were tuberculosis and mediastinal tumour; growths that start close to the hilum, beginning with early pressure signs, especially resemble growths of the mediastinum. Two cases were mistakenly diagnosed as carcinoma of the œsophagus, one as subphrenic abscess, and one as empyema. In two patients a primary pulmonary growth was unsuspected, since the clinical picture was entirely dominated by the neurological condition caused by the presence of secondary deposits in the brain. One presented a complete hemiplegia (growth in the right cerebral cortex), the other had epileptiform convulsions and coma without definite localising signs (growth in left cortex). One patient was thought to have an aortic aneurysm, and in one the growth—a very small "oat-celled" carcinoma—was discovered by chance at autopsy. The frequency with which these patients present themselves as "neurological cases," with symptoms due to metastases in the central nervous system, has been emphasised by Fried, who ascribes it to a hæmatogenous spread dependent upon the anatomical relations of the vessels of the lungs and brain. Of his 19 patients, 9 complained of nervous symptoms. Lubarsch [25] also described five cases in which the condition first showed itself through cerebral metastases, and Seyfarth [31] mentions as many as 32.

In 18 the correct diagnosis of intrathoracic neoplasm was made before death, but since the rarity of true mediastinal lymphosarcoma has been realised our difficulty lies less in determining the nature of the growth than in locating more precisely its site and point of origin. Unfortunately in this series no light can be thrown upon the prognostic difference between growths originating presumably in the bronchi themselves and those arising in the pulmonary alveoli.

Treatment.

The only treatment possible has been palliative; nearly all the patients were more comfortable propped up well forward in bed, and some ingenuity was often necessary to maintain them in a comfortable position. Deep X ray therapy in most cases produced temporary improvement and lessening of symptoms, but did not seem appreciably to check the course of the disease; severe transitory "reactions" occurred in two cases and very striking "remissions" in three. A more detailed list of these cases is shown in the table and a short bibliography of some papers on this subject is appended.

Summary.

1. Twenty-six cases of pulmonary carcinoma are described, 21 being histologically of the "oat-celled" type. 2. No distinction could be made clinically between the "oat-celled" type and lung tumours of polygonal, columnar, or squamous-celled type. 3. The ratio of men to women affected was, approximately, 3 to 1. 4. A somewhat marked incidence of previous lung affections, especially influenza and bronchitis, was found. 5. No connexion between the incidence of the growths and previous occupations could be traced. 6. Especially common modes of onset were (1) with pain in the chest alone; (2) with an acute febrile attack of "influenza" followed by a temporary return to work. 7. Early pressure signs were frequent, and should not necessarily suggest mediastinal tumour rather than a pulmonary growth. 8. The average age of the patients was 50, and the duration of the disease (from first symptom to death) was six months. 9. Hæmoptysis occurred in 48 per cent. and pleural effusion in 48 per cent. of these patients. 10. The position of the heart's apex was variable and was unaltered in 40 per cent. 11. Metastases were not a frequent cause of symptoms.

I should like to express my gratitude to Prof. F. S. Langmead, at whose suggestion this paper was prepared, for permission to examine the patients under his care and for his assistance in the consideration of the cases.

References.

1. Abraham, A.: Med. Klin., 1927, xxiii., 791.
2. Aschoff, L.: Path. Anat. Lehrbuch, Jena, 1914.
3. Barnard, W. G.: Cancer Review, 1926, i., 343.
4. Same author: Jour. Path. and Bact., 1926, xxix., 241.
5. Berblinger, W.: Klin. Woch., 1925, iv., 913.
6. Biberfeld, H.: Med. Klin., 1926, xxii., 1371.
7. Brandt, A.: Virchow's Arch., 1926, Bd. 262, p. 211.
8. Briese: Frankfurt. Ztschr. f. Path., 1920, xxiii., 48.
9. De la Camp, O.: Med. Klin., 1924, xx., 1270.
10. Duguid, J. B.: THE LANCET, 1927, ii., 3.
11. Dynkin, A.: Inaug. Diss. Basel, 1915 (Über die primären malignen Lungentumoren).
12. Edwards, A. T.: Brit. Jour. Surg., 1927, xiv., 607.
13. Ewing, J.: Neoplastic Diseases, London, 1927.
14. Ferenczy, K., and Matolcsy, T.: Wien. Klin. Woch., 1927, xl., 618.
15. Feyrter, F.: Ibid., 1927, xx., 649.
16. Fishberg, M.: Arch. Int. Med., 1926, xxvii., 445.
17. Fried, D.: Ibid., 1927, xl., 340.
18. Frommel, E.: Revue de Méd., 1927, xliv., i., 31.
19. Gruber, G. B.: Wien. Klin. Woch., 1928, xli., 1686.
20. Holzer, H.: Med. Klin., 1925, xxi., 1235.
21. Hudson, R. V.: Brit. Jour. Surg., 1926, xiv., 54.
22. Kirklin, B., and Patterson, R.: Amer. Jour. of Roentgen., 1928, xix., 20 and 126.
23. Kikuth, W.: Virchow's Arch. f. Path. Anat., 1925, Bd. 254, p. 107.
24. Lighty, J. A., Wright, F. R., and Baumgartner, E. A.: Jour. Amer. Med. Assoc., 1926, lxxxvii., 144.
25. Lubarsch, A.: Handbuch d. Spez. Path. Anat. und Histol., Berlin, Springer, 1925.
26. Rubenstone, A. I., Schwartz, M.: Med. Jour. and Rec., 1927, cxxvi., 719.
27. Sachs, I.: Schw. Med. Woch., 1924, xlvii., 1156.
28. Sauerbruch, F.: Zentralbl. f. Chir., 1926, liii., 852.
29. Schwyter, M.: Frankfurt. Ztschr. f. Path., 1928, xxxvi., 146.
30. Sehrt, E.: Inaug. Diss. Leipzig, 1904 (Beiträge zur Kenntniss der primären Lungencarcinome).
31. Seyfarth, C.: Deut. Med. Woch., 1924, l., 1497.
32. Shennan, T.: Jour. of Path. and Bact., 1928, xxxi., 365.
33. Sonnenfeld, A.: Med. Klin., 1928, xvi., 601.
34. Staehelin, R.: Klin. Woch., 1925, iv., 1853.
35. Wahl, S.: Ztschr. f. Krebsforsch., 1927, xxv., 302.
36. Wolf, K.: Fortschr. d. Med., 1895, xiii., 725.
37. Uspensky, A. E.: Ztschr. f. Krebsforsch., 1927–28, xxvi., 166.

BERKSHIRE CONTRIBUTORY SCHEME.—Last year £27,452 was collected by the Berkshire and Associated Hospitals Aid Committee, an increase over the preceding year of £3299, which constitutes a "record." The formation of five new branches partly accounts for this rapid growth. The expenditure on administration was £1407.

A POOR-LAW COUNTRY HOME.—The Birkenhead guardians have bought for £10,000 Sir Henry Vernon's residence, Eastham House, in the Wirral District, and have opened it as a home for aged and infirm poor and for convalescent patients from Tranmere Infirmary. The house which stands in 50 acres, has an oak-panelled staircase carved with scenes from *The Canterbury Pilgrims*.

OBSERVATIONS ON THE TREATMENT OF TWO CASES OF POLYCYTHÆMIA VERA WITH PHENYLHYDRAZINE HYDROCHLORIDE.

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FOR some time past it has been recognised that phenylhydrazine hydrochloride has the power of destroying red blood corpuscles, and it has been used by many investigators to produce anæmia in animals. Within recent years it has been exhibited for the same purpose in the treatment of polycythæmia vera. Eppinger and Kloss, while stating that there was an increased formation of red corpuscles in the bone-marrow in this disease, produced evidence to show that the process of red cell destruction was not so active as would be expected; therefore in 1918 they prescribed phenylhydrazine with the idea of stimulating the destruction of erythrocytes. They first administered the drug subcutaneously in solutions varying in strength from 1 per cent. to 10 per cent., but later they obtained the same results on giving the drug by the mouth. They considered this method of treatment to be an almost harmless means of reducing the number of red blood corpuscles and hæmoglobin. Since then it has been used by Taschenberg, Owen, Brown and Giffen, and others with very similar results. In all cases the red cells and hæmoglobin were diminished, while in some a moderate leucocytosis was produced. Jaundice appeared in the course of treatment, the urine became very dark in colour, and in a number of cases urobilin was present. It was noted by Owen, and Brown and Giffen that the red corpuscles continued to diminish in number for a varying period after the drug was stopped. In most of the cases reported the signs and symptoms of the disease returned in from two to six months, and the treatment had to be repeated. Taschenberg observed in his case that the desired effect did not always take place after repeated courses of treatment, and he thought that the drug might in some way harm the liver. Wells described lesions appearing in the liver when animals were poisoned with sulphate of hydrazine. Bodansky, working with phenylhydrazine, showed that it had a destructive action on the liver, and that variations in the lævulose-tolerance curve could be taken as an index of the toxic action of phenylhydrazine on the liver cells.

Recently we had the opportunity of treating two cases of polycythæmia vera with phenylhydrazine hydrochloride, and we resolved to record the histological changes in the blood. In the course of treatment certain other observations were made on changes taking place in the blood plasma, and in the resistance of the red cells to hypotonic saline.

CASE 1.—A male, aged 42, an engineer, first came under observation in 1922 complaining of giddiness, headache, and weakness in the legs which prevented him from working. The ears, lips, and tongue were cyanosed and the breath had a peculiar odour. The systolic blood pressure was 152 mm. of mercury, but the heart was not enlarged. The spleen could not be palpated, although the splenic area was enlarged to percussion. There was nothing of note in the past health or family history. The Wassermann reaction was negative. Three and a half months later the spleen was palpable at the costal margin. In August, 1925, the face, ears, lips, nose, and fingers had a deep crimson colour, and by December of that year the spleen could be palpated 1½ inches below the costal margin.

On admission in 1922 the red cells numbered 9½ millions, and from that date until readmission to hospital in April, 1927, the red cells varied between 7 and 9 millions. During these five years he had been taking benzol by mouth more or less continuously.

On April 26th, 1927, he was readmitted. He had been unfit for work, and on examination the cardiac area was found to be slightly larger than normal and the radial arteries palpable. The spleen reached forwards and down-

wards to the level of the umbilicus 1 inch from the middle line, and the red cells numbered 9 millions. He was given grs. 2 of phenylhydrazine hydrochloride twice daily and, on three occasions at weekly intervals, 7 oz. of blood were withdrawn from one of the veins of the arm. In four weeks the red corpuscles were reduced to 5 millions and he was dismissed from hospital feeling very well. He reported frequently and phenylhydrazine hydrochloride was prescribed from time to time, as the blood count indicated, in doses varying from gr. ½ to grs. 2 twice daily. By May, 1928, the red cells numbered 6½ millions and, as he was not feeling fit, he was again readmitted for observation on May 25th. He was treated with a fresh supply of phenylhydrazine hydrochloride, for it was thought that the old stock had deteriorated and was not having the desired effect. This ultimately proved to be the case. The following table shows the dosage given and the response obtained after admission to hospital on May 25th, 1928.

TABLE I.—*Selected Blood Counts in Case 1.*

Days after admission.	Red blood cells, millions	White blood cells.	Hæmoglobin, per cent.	Colour-index.	Blood-platelets.	Reticulocytes, per cent.
3	6·6	17,000	100·0	0·76	332,000	Nil.
6 (*a*)	6·4	16,600	107·0	0·82	—	„
8	6·9	19,600	120·0	0·87	604,000	„
9 (*b*)	—	—	—	—	—	—
11	5·7	22,400	98·5	0·86	573,000	Nil.
13 (*c*)	5·4	28,400	87·0	0·79	334,890	8·0
15	5·0	26,700	80·0	0·8	503,000	3·8
17	4·4	26,600	65·0	0·74	—	—
18 (*d*)	4·4	41,000	62·5	0·71	769,700	4·0
19	4·1	29,800	60·0	0·75	—	3·9
21	3·5	22,600	62·5	0·8	518,520	5·0
22 (*e*)	—	—	—	—	—	—
23	3·2	22,400	56·0	0·87	—	4·0
25	3·7	20,200	55·0	0·74	—	8·0
28	3·3	17,400	52·0	0·78	—	1·0
32	4·2	20,200	60·0	0·71	—	4·0
39	4·0	19,400	68·0	0·86	—	3·0
46	4·8	25,000	76·0	0·8	—	—
60	5·2	16,800	112·0	1·07	—	—
90 (*f*)	9·1	13,000	110·0	0·6	—	—
98	6·1	20,000	110·0	0·9	—	—
102	6·7	24,600	125·0	0·9	—	—
109	6·6	21,000	106·0	0·8	—	—
116 (*g*)	4·4	21,800	77·5	0·88	—	—
130	4·6	22,600	90·0	1·0	—	—
152	5·8	10,400	115·0	0·99	—	—

(*a*) Phenylhydrazine hydrochloride grs. 1½ given t.i.d.
(*b*) „ „ grs. 3 „ b.i.d.
(*c*) „ „ grs. 1½ „ t.i.d.
(*d*) „ „ stopped.
(*e*) Dismissed from hospital.
(*f*) 15 oz. blood removed by venesection. Phenylhydrazine hydrochloride grs. 3 given daily.
(*g*) Phenylhydrazine hydrochloride stopped.

CASE 2.—A male, aged 74, an artist by profession, was admitted to hospital after a hæmatemesis which had occurred 14 days previously. On other occasions he had vomited blood, and one year earlier he had had a hæmaturia, cystoscopic examination at this time failing to reveal any cause for the bleeding beyond some congestion of the prostatic venous plexus. Six months later he had developed phlebitis in both legs. For the past 15 or 20 years he had been subject to attacks of indigestion. The face and lips were well coloured, but there was no cyanosis. The area of cardiac dullness was within normal limits, but the spleen extended downwards to about three inches below the costal margin. The Wassermann reaction was negative. The dosage of phenylhydrazine hydrochloride given and some of the changes observed in the blood are shown in Table II.

The phenylhydrazine hydrochloride was given in gelatin capsules and administered by mouth, the amount varying from grs. 4½ to grs. 6 daily. Usually the dose prescribed was grs. 1½ thrice daily to begin with, then it was increased to grs. 3 twice daily until the red corpuscles began to fall in number, when the dose was reduced to grs. 1½ thrice daily. This was continued until the red cells numbered about 4½ millions, when the drug was discontinued. In Case 1 the total amount of phenylhydrazine hydrochloride prescribed over a period of 12 days was grs. 63, and in Case 2, in 20 days, grs. 103½ were administered. The red cells began to decrease in number in the first case after grs. 19½ had been given, while the second case required grs. 79½ before any response was evident. It therefore appears that some individuals respond more quickly than others to the treatment, but it should be noted that Case 1 was aged 48, and Case 2 aged 74. The exhibition of the drug was controlled by frequent blood counts and, in view of its toxic action on the liver cells, as shown by Wells and

TABLE II.—*Selected Blood Counts in Case 2.*

Days after admission.	Red blood cells, millions	White blood cells.	Hæmoglobin, per cent.	Colour-index.	Blood-platelets.	Reticulocytes, per cent.
4	7·6	9,800	87·5	0·57	421,740	—
5 (*a*)	—	—	—	—	—	—
7	8·0	10,600	91·0	0·54	478,800	0·5
9	7·4	11,800	92·5	0·65	—	0·1
11 (*b*)	8·3	9,900	106·0	0·64	—	1·0
13	7·7	9,000	95·0	0·63	689,400	1·0
15	7·3	10,600	81·0	0·55	—	1·0
17	7·7	11,600	92·0	0·6	—	—
20	6·2	14,000	75·0	0·6	820,610	3·5
21 (*c*)	—	—	—	—	—	—
22	5·4	13,600	72·0	0·67	—	5·0
24 (*d*)	4·3	16,400	55·0	0·64	988,200	4·4
26	3·0	16,200	62·5	1·04	—	—
29	2·7	16,400	45·0	0·86	—	8·0
31	2·7	13,000	50·0	0·92	—	15·0
35	2·8	7,000	68·0	1·02	—	6·0
42	3·6	6,800	77·5	1·07	217,200	—
49	4·1	6,000	100·0	1·2	—	—
55 (*e*)	—	—	—	—	—	—
124	5·7	—	110·0	0·9	—	—

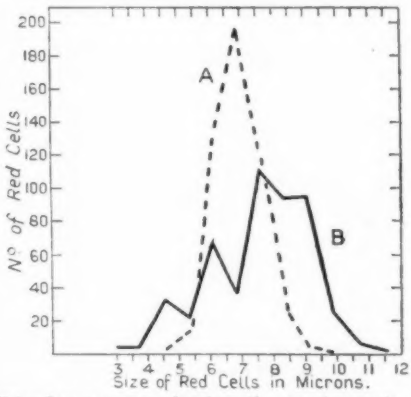
(*a*) Phenylhydrazine hydrochloride grs. 1½ given t.i.d.
(*b*) „ „ grs. 3 „ b.i.d.
(*c*) „ „ grs. 1½ „ t.i.d.
(*d*) „ „ stopped.
(*e*) Dismissed from hospital.

Remarks.—Fourth and thirteenth days after admission: bilirubin less than 0·25 units. Twentieth day: bilirubin 0·5 units. Twenty-fourth day: bilirubin 1 unit.

Bodansky, lævulose-tolerance curves were made before, during, and after treatment. The curves obtained were never indicative of hepatic inefficiency.

Effects on the Blood.

From the tables of blood counts it will be seen that the red cells became reduced in number, and that the diminution continued for some time after the drug was stopped, for a period of ten days in the case of the first patient and five days in the second patient. The latter at first responded very slowly to the action of the phenylhydrazine, but when the red cells did begin to decrease they did so very rapidly, falling from 7·7 millions to 2·7 millions in 12 days. At first the fall in the percentage hæmoglobin was more or less parallel with the fall in the number of red cells, but as the anæmia became more profound, and later when the red corpuscles were beginning to increase in number, there was an increase in the colour-index. This was most noticeable in Case 2. On the twenty-ninth day after admission there was an increase in the mean



Price-Jones curves showing the greater variation in size and an increased proportion of large red cells in the circulation three days after treatment had been discontinued. A is the curve obtained the second day after admission—i.e., before treatment. Mean diameter of red cells 6·95 μ. B is the curve on the twenty-ninth day after admission. Mean diameter of red cells 7·72 μ.

diameter of the red cells as compared with the mean diameter before treatment was commenced.

Examination of blood films from day to day showed the gradual appearance of nucleated red cells (normoblastic in type), reticulocytes, polychromasia, poikilocytosis, and anisocytosis, all of which became more marked as the anæmia became more profound. An increasing proportion of the red cells were megalocytes, and as time went on the blood gradually assumed a megalocytic character. This is shown graphically in the figure, in which two curves, plotted after the fashion of Price-Jones, show the differences in size (mean diameter), and the alteration in the proportion of cells of various sizes, between 500 red cells on the second day of admission—i.e., immediately before treatment was commenced, and another 500 red cells on the twenty-ninth day—i.e., three days after the phenylhydrazine had been discontinued.

There was a tendency for the blood platelets to increase in number during treatment, and the reticulocytes increased as the anæmia became more marked. While the phenylhydrazine hydrochloride was being given there was a progressive leucocytosis in each case, but as soon as the drug was discontinued the white cells immediately began to return to the level, or even below the level, at which they had been before treatment started. The leucocytosis was entirely due to cells of the granular series, particularly the neutrophil polymorphonuclear leucocyte. There was, however, a slight percentage increase in the number of basophil and eosinophil polymorphonuclear cells. In each case there was an absolute and relative diminution in the number of lymphocytes.

In the course of treatment jaundice appeared, first in the scleræ and a few days later becoming generalised over the body, but it was always slight. The van den Bergh reaction was never of the direct type, and the indirect reaction showed a gradual increase in the bilirubin content of the blood serum as the jaundice became more widespread. (Tables II. and III.) After treatment was discontinued, the icterus cleared up within a few days in each case. Table III. also shows the changes in the blood nitrogen and the blood cholesterol in Case 1. There was a slight increase in the former while the plasma cholesterol fell from 160 mg. per 100 c.cm. to 70 mg. per 100 c.cm. during the administration of the drug.

TABLE III. (*Case 1.*)

Days after admission.	Blood.						
	Red blood cells, millions	Bilirubin, units.	Cholesterol (plasma), mg. per 100 c.cm.	Nitrogen.		Urinary urea, per cent.	Urobilin.
				Urea.	N.P.N.		
				mg. per 100 c.cm.			
3	6·6	(under 0·25)	—	—	—	—	—
4	—	—	160	11·0	33·0	—	—
5	—	—	—	—	—	1·8	—
6 (*a*)	6·4	—	—	—	—	—	—
7	6·9	0·25	—	—	—	1·7	—
11	5·7	(more than 0·25)	100	—	—	2·3	—
13	5·4	—	—	23·2	45·0	2·2	—
14	4·9	1·2	126	—	—	2·7	—
16	4·7	2·0	—	—	—	2·7	—
18 (*b*)	4·4	3·0	70	24·2	45·0	2·6	+
21	3·4	1·5	80	22·0	50·0	2·4	—
60	5·2	0·25	118	—	—	—	—

(*a*) Treatment commenced. (*b*) Treatment stopped.

Observations on the fragility of the red cells did not reveal anything unusual in Case 2, but in Case 1 on the third, fourth, and seventh days lysis commenced in 0·45 per cent. salt solution, on the eleventh day in 0·35 per cent. salt solution, and on the fourteenth and eighteenth days in 0·4 per cent. salt solution. Lysis was invariably complete in 0·3 per cent. salt solution. It appears, therefore, that there was a tendency to some slight increase in resistance to hypotonic saline solution. In the experimental anæmias produced in animals by phenylhydrazine the red cells show an increased resistance to lysis in hypotonic salt solution (Muir). Taschenberg noted in his case that, with each successive course of treatment, more phenylhydrazine was required to bring about a reduction in the number of red cells, which reacted normally to hypotonic salt solution; he concluded that the red corpuscles acquired a special resistance to phenylhydrazine. No definite statement can be made about this, but Case 1 has had phenylhydrazine at intervals over a period of 16 months, and still reacts to suitable doses of the drug, provided it is fresh.

During the treatment of both patients the most remarkable change found in the urine was in its colour, which became very dark and at times almost black. The nature of this change is not understood. Urobilinogen was never found, and positive tests for urobilin were obtained only in Case 1 on three occasions—on the seventeenth, eighteenth, and nineteenth days after admission. There was a gradual increase in the output of urinary urea from 1·7 per cent. before treatment to 2·7 per cent. after treatment in Case 1, and in Case 2 the urea increased from 2·1 per cent. to 2·7 per cent.

Complications.

While in hospital, Case 1 became free from his symptoms as the red cells were reduced and no complications arose, despite the fact that he was allowed up while the phenylhydrazine was being given. He was dismissed on the twenty-second day feeling fit and well. The red cells at that time numbered 3·2 millions. No alteration was noted in the size of the spleen. Ten days afterwards he complained that his right ankle was swollen, red and tender, and the same thing occurred in the left ankle nine days later. At this time no phenylhydrazine was being administered. No phlebitis was observed, and the swelling and pain in the joints cleared up satisfactorily with a few day's rest. The red cells gradually increased until, on the ninetieth day after admission, they numbered 9·1 millions. He complained of flushing of the face, pains in the head, and tingling of the fingers. Fifteen ounces of venous blood were withdrawn, and he was given phenylhydrazine hydrochloride grs. 3 daily. A week afterwards the red cells were 6·1 millions, and the drug was continued until in another 18 days the red cells had fallen to 4·4 millions, when it was stopped. The red cells are again increasing, and it is anticipated that before long the patient will require another course of treatment. After treatment had been stopped, but while he was still in hospital, Case 2 developed a phlebitis in the right great saphenous vein on the twenty-ninth day after admission, when the red cells were 2·6 millions. This took some time to clear up, and he was not dismissed from hospital until one month later. When he reported ten weeks later the red cells numbered 5·7 millions, but he was keeping remarkably well and free from symptoms. No further doses of phenylhydrazine have yet been prescribed.

The above findings agree more or less closely with those reported from time to time by the other observers. Taschenberg, and Brown and Giffen mention the occurrence of thrombosis during treatment, but, as the latter writers also point out, thrombosis is common in cases of polycythæmia vera without treatment. It is a noteworthy fact that in Taschenberg's case and in our Case 2 there was a previous history of thrombosis and hæmatemesis. Brown and Giffen suggest that under treatment there is liberation of thromboplastic material which might predispose to thrombosis. In this connexion it is interesting to note the statement by Rosenthal regarding the blood-platelet factor and splenectomy. He points out the relationship between thrombosis and an increased platelet count in certain cases showing Banti's syndrome, and he mentions one such case in which, after excision of the spleen, the platelets rose to over 1 million and thrombosis supervened.

After this there was a diminution in the number of platelets. In Case 2 the platelets numbered 988,200 five days before the onset of the phlebitis; 13 days afterwards the platelets numbered only 217,200. Brown and Giffen also mention the possibility of a platelet factor being associated with thrombosis but, in three of their cases in which the blood-platelets were counted, the count was normal in two, while in the third the count was high at the beginning of treatment and gradually diminished to normal.

The question of possible damage to the liver from poisoning by phenylhydrazine is regarded as important by most of the other observers, mainly on account of lesions produced in the liver in experimental work on animals with hydrazine compounds, and also on account of the hepatic cirrhosis found on post-mortem examination in the case of polycythæmia reported by Levi, which had been treated with phenylhydrazine for one and a half years. But it is well known that cirrhosis of the liver may occur as a late complication in polycythæmia vera where no phenylhydrazine has been given. Levi considers that the cirrhosis is related to destruction of red cells, and that where phenylhydrazine is administered this destruction is increased and may hasten the onset of cirrhosis. Owen is inclined to regard the leucocytosis as an early sign of toxic damage to the liver cells, and therefore advises that treatment be discontinued if the leucocytosis becomes markedly increased. In the seven cases treated by Brown and Giffen, and in the two cases recorded above in which various tests of hepatic efficiency were carried out, no evidence of liver damage was found. Perhaps sufficient time has not yet elapsed to judge the effect of repeated courses of treatment, but Case 1, after six courses of phenylhydrazine within 16 months, shows no sign of hepatic inefficiency and, indeed, is now able to do light work as a night watchman.

Conclusion.

There seems to be no doubt that phenylhydrazine given by mouth is an effective agent in bringing about destruction of red cells. It is not known whether the destructive process is intracellular or extracellular in nature, but evidence of the hæmolytic effect of the poison is afforded by the increasing bilirubin content of the blood serum and the occasional appearance of urobilin in the urine. The action on the hæmopoietic system is not clear. From the experimental anæmias produced in animals phenylhydrazine appears to inhibit regeneration of the blood cells in some way. While that may be so, the data given above indicate, in the case of the erythropoietic system, an active regeneration rather than an inhibition. This is shown by the early appearance of reticulocytes, megalocytes, and polychromasia. Whether this activity is due to direct stimulation of the erythropoietic tissues, or whether it is secondary to the red cell destruction, cannot be definitely stated, but it is probable that the increased activity is a response to the demand for red cells to replace those destroyed by the phenylhydrazine. In common with many other drugs and poisons, phenylhydrazine seems able to call forth a leucocytosis, and this is thought to be due to some chemiotactic influence stimulating directly the leucoblastic tissues.

While the beneficial action of phenylhydrazine hydrochloride is only temporary, its use in the treatment of polycythæmia vera is justified by the feeling of well-being and the freedom from symptoms which it produces, always provided that its exhibition is controlled by frequent blood counts, and that it is discontinued when the number of red cells reaches the neighbourhood of 4·5 millions. While as yet there is no definite contra-indication, it must always be remembered that phenylhydrazine hydrochloride is a protoplasmic poison, and should be used, therefore, with care and respect.

I gratefully acknowledge my indebtedness to Prof. W. K. Hunter for permission to treat these two cases and publish the results. My thanks are also due to Dr. C. M. Fleming for her kindness in carrying out the blood nitrogen and blood cholesterol estimations mentioned in Table III.

References.

Eppinger, H., and Kloss, K.: Therap. Monats., 1918, xxxii., 322.
Taschenberg, E. W.: Deut. med. Woch., 1921, xlvii., 774.
Owen, T.: Johns Hopkins Hosp. Bull., 1924, xxxv., 258.
Same author: Jour. Amer. Med. Assoc., 1925, lxxxv., 2027.
Brown, G. E., and Giffen, H. Z.: Arch. Int. Med., 1926, xxxviii., 321.
Wells, H. G.: Jour. Exper. Med., 1908, x., 457.
Bodansky, M.: Jour. Biol. Chem., 1923–24, lviii., 799.
Price-Jones, C.: Jour. Path. and Bact., 1922, xxv., 481.
Muir, R.: Text-book of Pathology, London, 1925, p. 350.
Rosenthal, N.: Jour. Amer. Med. Assoc., 1925, lxxxiv., 1887.
Levi, E.: Zeit. für Klin. Med., 1924, c., 777.

PITUITARY CACHEXIA IN A CASE OF TABES DORSALIS.

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WITHIN recent years a great deal of attention has been paid to an affection of the pituitary gland, described as "Simmonds's disease," or "pituitary cachexia." The nosology of the glands with internal secretion is so complex and their physiology so incomplete, in spite of the overwhelming volume of literature on the subject, that a brief outline of Simmonds's disease seems justified. In 1914 Simmonds [1] described a case of total necrosis of the anterior, i.e., glandular part of the pituitary gland, caused by a post-partum septic embolus in the arterial supply of the lobe, which is separate from the supply of the posterior lobe. The most outstanding clinical feature was an extreme cachexia, accompanied by a senile aspect, loss of axillary and pubic hair, general nervous disturbances, and reduction in size of the abdominal organs (microsplanchnia). The atrophy of the anterior lobe can be caused by a variety of processes, such as compression through cysts and tumours, functional exhaustion through pregnancy, as claimed by Maresch [2] and Budde,[3] tuberculous infection, as described by Schlagenhaufer,[4] and, probably most important of all clinically, luetic affections. A number of cases of the last-named are reviewed by Jaffé,[5] and a general survey is to be found in the work of Kraus [6] and others. The symptomatology of the disease, excellently described by Redlich,[7] is very wide, though some salient features seem to be unmistakable. Trophic-vasomotor changes of the skin, as in myxœdema and sclerodermia, as well as in numerous cases total loss of teeth without caries, have been mentioned by Graubner,[8] Reye,[9] and Zondek.[10] Stress has been laid, as mentioned before, on the loss of hair under the armpits and pubic hair, as well as on the loss of hair on the trunk, while the growth of hair on the head and face remained unaffected. In our case there was a distinct loss of hair on the head, while the rest remained comparatively intact.

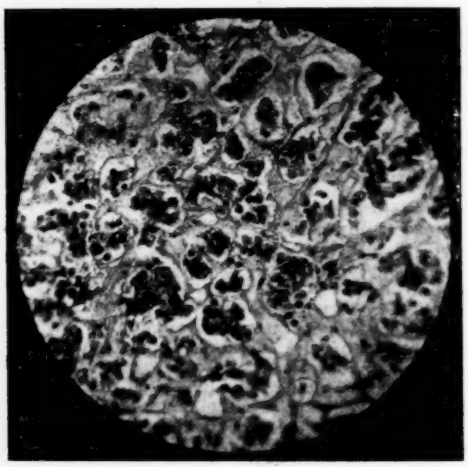
One might summarise the majority of symptoms under the heading of "hypofunction"; the pronounced muscular weakness, low body temperature, low blood pressure, and lowering of hæmoglobin, sometimes accompanied by marked eosinophilia. Lowering of basal metabolism, water- and mineral-metabolism, and particularly disturbances of sodium chloride excretion, are reported by various authors. Cessation of the menses in women and a premature senility in both sexes, caused by atrophy of the genital organs, are almost constantly described. The nervous and psychological symptoms are dominated

by a certain torpor and apathy, very often coupled with marked sleepiness, which is, as repeatedly mentioned by Cushing, a frequent occurrence in pituitary tumours as well as after experimental removal of the pituitary gland. The neuro-psychological symptoms are so marked and constant that such an experienced observer as Redlich (loc. cit.) tentatively suggests the term of "præ-hypophysial depression." Narcolepsy in Simmonds's disease has been described by Pennetti.[11] Jakob [12] has described two cases of Simmonds's disease where a careful histological examination of the brain failed to reveal any signs of the pathological changes of presbyophrenia or Alzheimer's disease, which tends to show a certain independence in the causation of the presenile changes.

The theoretical aspect of pituitary pathology is very controversial and complex and cannot be gone into here. Three separate possibilities and their combination seem to form the basis of an attempt to understand and explain the clinical pathology of the pituitary disorders: (1) The impairment of independent glandular activity of the pituitary gland, considered as a whole or in its parts—i.e., of anterior, posterior, and intermediate lobe. The anatomical and physiological existence of the last-named in man is doubtful and controversial. (2) The correlation and interaction of the effective pituitary gland within the system of glands of internal secretion. (3) The relation of the disease to the subthalamic centres in the mid-brain.

Several authors, like Biedl, Cushing, and others, hold that there is a close relationship between Simmonds's disease and the syndrome first described by the French as "insuffisance pluriglandulaire." Good therapeutic results from the ingestion of anterior-lobe preparations are claimed by Reye, Nonne, Lichtwitz, and others. Amongst the numerous

FIG. 1.



Section of anterior lobe of pituitary gland, showing fibrotic atrophy. Hæmatoxylin-eosin stain.

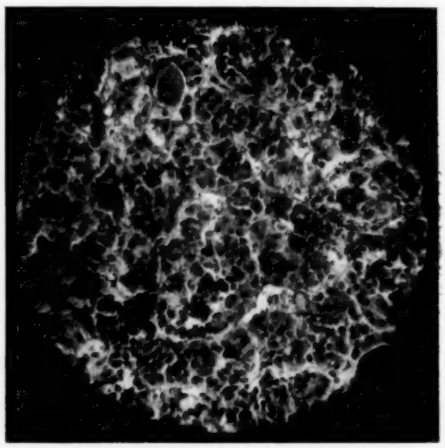
contributions to the literature of the subject may be mentioned certain papers to which reference is made in the bibliography.[13-25]

Report of Case.

A woman of 37 was admitted from Woodstock Workhouse Infirmary on Oct. 23rd, 1922. She was moody, sullen, and quarrelsome, threatened to "finish herself," got out of bed at night, and tried to get at the knives. She was stated to have been feeble-minded to a moderate degree since childhood and to have had illegitimate children. She became a charge to the workhouse. The family history was unobtainable. There was no history of miscarriages. At the time of admission no marked pathological changes were found in the internal organs. There was a slight parenchymatous struma and double optic atrophy. Both knee-jerks were absent and both ankle-jerks present. There was no light reaction in the pupils, and the Wassermann reaction was positive.

The depression seemed to clear up, and the patient became orientated and quiet, and her bodily condition improved.

FIG. 2.



Section of anterior lobe of pituitary gland of an abortive case of dystrophia adiposo-genitalis (Fröhlich's disease) with well-developed glandular tissue. Hæmatoxylin-eosin stain.

On March 23rd, 1924, she was discharged to the workhouse, whence she was readmitted on August 10th, 1927. She was then bedridden, and had apparently been very restless for some time. She said that "strong feelings came over her, and then for a time she did not know where she was," "that she intended to make away with herself." She had bedsores on the buttocks and a small abrasion on the outer aspect of the left knee. The knee- and ankle-jerks were absent, but there was no Babinski sign. There was marked ataxia. The globulin in the cerebro-spinal fluid, tested by Pandy's method, was + +, and the Lange gold-sol reaction gave a tabetic curve. She had shooting pains and gastric crises with repeated vomiting only relieved by morphia. She was very restless and agitated at times, and had persistent constipation. On Nov. 4th, 1927, she was inoculated with malaria by mosquitoes. On Nov. 19th she had her first rigor, and her temperature went up to 104° F. The second rigor was on Nov. 21st, when the temperature rose to 105° F. On Nov. 23rd she was given quinine, as her condition was not favourable to more rigors, and no more occurred. On March 26th, 1928, she showed no physical improvement, had a series of abscesses on the buttocks, and was mentally very lethargic. A month later she was very emaciated and showed a progressive loss of hair from her head. She had an almost voracious appetite. On May 21st a perforating ulcer had developed on the right hip; on account of her extreme emaciation the capsule of the joint was exposed to view. There was also an ulcer on the left hip. On June 2nd she was weaker and incontinent, and on June 7th, at 3.55 A.M., she died.

Post-mortem Report.

Extreme emaciation. No external injuries. Perforating bedsores at both trochanters and along the proximal part of the pelvis. Skull symmetrical, eburnation of diploë, diameter about 8 mm. Almost complete ossification of sutures. Adhesion of dura mater to skull-cap. Pia-arachnoid thickened, adherent to convolutions. Convolutions flat, sulci shallow, more marked in fronto-parietal region. Consistence of brain and spinal cord softened, paste-like. Degeneration of posterior columns in spinal cord from beginning of sacral segments to lower cervical segments. Microscopically, besides loss of medullated fibres in posterior root-zones, marked endarteritis luetica throughout the central nervous system.

Adhesions at both pulmonary apices. Acute inflammatory process on the left lower lobe of the lungs with marked œdema. Heart not enlarged, tricuspid and mitral valve

show some fibrotic changes, possibly of syphilitic origin. Several atheromatose plaques and one scar about 4 mm. in length in the arch of the aorta. Sclerotic changes in both coronary arteries. Fatty degeneration and partial atrophic changes in the liver. Gall-bladder normal. Bile-ducts patent. Atrophic changes in the mucous membrane of the stomach and intestine. Parenchymatous nephritis. Spleen slate-grey with perisplenitis, showing Malpighian corpuscles and increase of trabeculæ on cross-section; slightly enlarged. Pancreas and suprarenal bodies without marked changes. Parenchymatous struma to a moderate degree. Retrogressive changes of uterus and ovaries. Anterior lobe of pituitary gland (Fig. 1): very extensive fibrosis with consecutive reduction of glandular tissue to small irregularly scattered islets. Almost complete disappearance of eosinophil cells, basophil cells slightly increased, some "main" cells well preserved. Almost complete disappearance of vessels. Absence of colloid cysts in pars intermedia.

Posterior lobe: Apart from a slight gliosis and reduction in size, no pathological changes seen. Capsule irregularly thickened. Fig. 2 shows a well-developed anterior lobe for comparison.

Oppenheim mentions in his "Text-book of Nervous Diseases" (1913, vol. i., p. 186) that he saw two cases of tabes dorsalis in which, besides a local muscular atrophy, a striking general marastic (cachectic) condition was a feature, and adds that he feels justified in supposing, from his own experience, that general emaciation may be a symptom of the disease, that a rare form ("marantic tabes") exists which is characterised by an early, considerable general emaciation; he adds an illustration of one of his cases (Fig. 184). A spontaneous loss of teeth without caries in tabes dorsalis is also described in the same text-book (p. 181).

We venture to suggest that these are pituitary symptoms in the meaning of Simmonds's disease.

Summary.

The case considered on the whole shows a fairly typical course of tabes dorsalis. Within about three months of the patient's death rapid emaciation set in, which was accounted for at the post-mortem examination by a fibrous atrophy of the anterior lobe of the pituitary gland—Simmonds's disease. It is not unlikely that when more attention is directed to the possibility of this condition a greater number of cases will be clinically diagnosed. Attempts at organotherapeutic treatment seem to be indicated.

References.

1. Simmonds, M.: Deut. med. Woch., 1914, xl., 322; 1916, xlii., 190; 1918, xliv., 852.
2. Maresch, R.: Verhandl. d. pathol. Ges., 1914, xvii., 212.
3. Budde, M.: Frankfurt. Zeit. f. Path., 1921, xxv., 16.
4. Schlagenhaufer, F.: Virchows Arch., 1916, ccxxii., 249.
5. Jaffé, R.: Frankfurt. Zeit. f. Path., 1922, xxii., 324.
6. Kraus, E. J.: In Kraus-Brugsch Handb. d. Path. u. Ther., vol. i., and Handb. d. allgem. Path., vol. viii., 905; Frankfurt. Zeit. f. Path., 1927, xxxv., 495.
7. Redlich, E.: Jahrb. f. Psychiat. u. Neur., 1927, xlv., 276.
8. Graubner, W.: Zeit. f. klin. Med., 1925, ci., 249; Med. Klinik, 1920, xvi., 1317.
9. Reye: Deut. Zeit. f. Nervenheilkunde, 1921, lxviii.-lxix., 153; Münch. med. Woch., 1925, lxxii., 155; Deut. med. Woch., 1928, liv., 696.
10. Zondek, B.: Diseases of Endocrine Glands, 2nd edition, 1926, p. 227.
11. Pennetti, G.: Riforma Med., 1928, xliv., 9.
12. Jakob, A.: Virchows Arch., 1923, ccxlvi., 151.
13. Kiyono, H.: Ibid., 1926, cclix., 388.
14. Benda, C.: Verh. d. deutschen pathol. Ges., 1927, xxii., 185.
15. Kraus, E. J., and Traube, O.: Virchows Arch., 1928, cclxviii., 315.
16. Rasmussen, A. T.: Endocrinology, 1928, xii., 129.
17. Berblinger, W.: Frankfurt. Zeit. f. Pathol., 1927, xxxv., 497.
18. Mogilnitzky, B.: Virchows Arch., cclxix/xi., 1.
19. Hallion, L.: Rev. prat. de biol., 1927, xx., 33.
20. Collin, R.: Rev. franç. d'Endocrinol., 1925, iii., 277.
21. Roussy, G.: Ann. de Méd., 1925, xviii., 407.
22. Veit, B.: Frankfurt. Zeit. f. Pathol., 1922, xxviii, 1.
23. Oppenheim, H.: Lehrb. d. Nervenkrank., 1913, i., 186.
24. Holmes, G., and Dott, N. M.: Brit. Med. Jour., 1926, ii., 1035.
25. Simmonds, J. I., and Brandes, W. W.: Arch. Path. and Lab. Med., 1926, ii., 18–22.

DIGESTIVE ENZYMES OF THE HUMAN FŒTUS.

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MANY observations have been made at various times upon the external secretions of the human fœtus, and the time of the first appearance of the different digestive enzymes is very variously quoted by different investigators,[1 2] many of whom have reported upon a few specimens only. As this problem is peculiarly one in which varying external conditions may vitiate the finding, the resulting experimental error in observation can be eliminated only by examining a very large series of cases under conditions as constant as possible. The present paper is based on the examination of 39 fœtuses, admittedly a small number, but dependable because only absolutely fresh material was used. The fœtus was considered as fresh only when received within 12 hours of birth, when it had died during or after parturition and not previously, and when on post-mortem examination it showed no autolytic change. Unfortunately no material suitable for enzyme-testing was obtained earlier than the sixteenth week, so that these observations extend only over the period from 16 weeks to full time.

Methods.

Histological.—Material was fixed either in formalin (5–10 per cent. in NSS), or formo-acetic Muller (formalin 5, glacial acetic acid 5, Muller's fluid 90), and embedded in paraffin wax. Sections were stained by Scott's hæmatoxylin and Biebrich scarlet, by Mallory's aniline blue-orange G mixture, and by Weigert's resorcin-fuchsin method. The sections were mounted in Gurr's neutral mounting medium or Canada balsam.

Chemical.—The fresh organ was quickly washed free from blood, chopped up finely, and extracted in about 10–15 times its volume of 90 per cent. glycerine in an incubator at 37° C. for 12 hours. The extracts were then filtered and tests were performed for various enzymes as follows. The quantities given represent the proportions and not necessarily the actual amounts used.

(*a*) *Amylase* (salivary and pancreatic). 1 c.cm. of 1 per cent. starch solution + 1 c.cm. extract (submaxillary or pancreas) + a trace of 1 per cent. sodium carbonate. Incubate at least two hours. Test with weak iodine for erythrodextrin.

(*b*) *Pepsin.* 1 c.cm. of 0·2 per cent. hydrochloric acid + 1 c.cm. extract (stomach) + washed fibrin. Incubate at least two hours; boil; filter. Test filtrate by xanthoproteic or Biuret test for proteoses.

(*c*) *Rennin.* 1 c.cm. milk that has been just brought to boiling-point and then cooled + 1 c.cm. extract (stomach) + trace of hydrochloric acid. Incubate at least one hour. Examine for formation of curd.

(*d*) *Trypsin.* Test as for pepsin, but using pancreas extract and adding 1 c.cm. K_2HPO_4 solution[3] instead of hydrochloric acid.

(*e*) *Erepsin.* Test as for trypsin but using duodenal extract.

(*f*) *Lipase.* 1 c.cm. of boiled milk + ½ c.cm. of 2 per cent. bile-salt solution, + 1 drop phenolphthalein, + 1 c.cm. extract (pancreas) + enough 1 per cent. sodium carbonate to render pink. Incubate at least two hours. Examine for neutralisation of alkali as shown by loss of colour.

(*g*) *Lactase.* 1 c.cm. of 1 per cent. lactose, + 1 c.cm. extract (duodenum). Incubate at least two hours. Test for glucose by Barfoed's test.

(*h*) *Invertase.* 1 c.cm. of 1 per cent. cane-sugar, + 1 c.cm. extract (duodenum). Incubate at least two hours. Test for glucose by Benedict's test.

[1] Feldman, W. M.: Antenatal and Postnatal Child Physiology, 1920, pp. 178–185.
[2] Hammar, J. A.: Uppsala läkareförenings förhandlingar, n.f., 1925, xxx., 151.
[3] Cole, S. W.: Practical Physiological Chemistry, Cambridge 1926, p. 28. Series C. pH = 7·9.

(*i*) *Maltase.* 1 c.cm. of 1 per cent. maltose + 1 c.cm. extract (duodenum). Incubate at least two hours. Test for glucose by Barfoed's test.

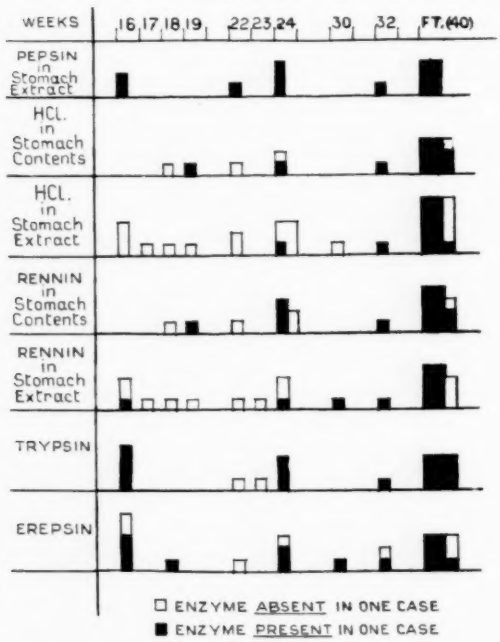
In every case a control experiment was carried out, the organ extract being first boiled. In addition, hydrochloric acid was tested for by Günzberg's test. Some tests were carried out for the presence of enterokinase and trypsinogen, but the method appeared to us open to criticism, and the results are not here recorded. In a few cases the contents of the stomach were pipetted off and tested separately, an extract being subsequently made of the washed gland, and also tested.[4]

Salivary Glands, Stomach, and Small Intestine.

Ptyalin (salivary amylase) was tested for in 19 cases, from 17 weeks upwards; its presence was detected in 5 only out of 12 full-time fœtuses. No trace was found in earlier extracts (see Chart 2). No chemical tests were carried out for the other constituents of saliva, but from the microscopic structure of the glands mucin was probably present. Definite mucin-secreting cells are found at 24 weeks, and the ducts contain a basophil mucin-like material. Previous to this (16 weeks) a similar material is seen in the lumen.

Pepsin was found in every case tested—namely, 13—varying from 16 weeks up to full time. Rennin was found in the gastric contents in 18 out of 23 cases, the earliest being 19 weeks. In the extract of the mucous membrane rennin was found in 12 out of 24, once at 16 weeks, and then not until 24 weeks (see Chart 1).

CHART 1.

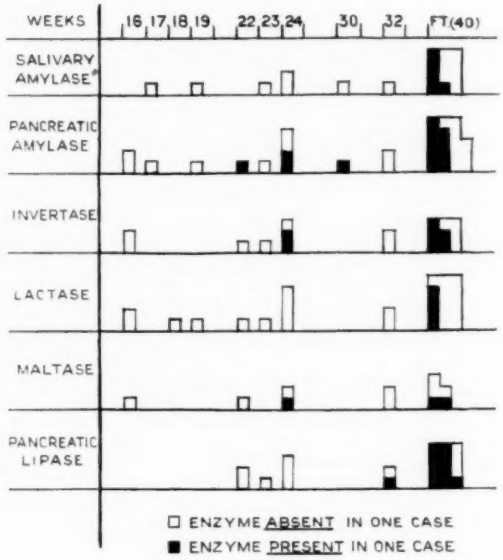


Hydrochloric acid, as tested by Günzberg's reagent, was found in the stomach contents (15 specimens), the earliest at 19 weeks, and eight out of nine times at full time. In the extract hydrochloric acid was not found so early, being present first at 24 weeks (once out of 14 tested up to and including this age); at full time it was found in 11 out of 15 specimens (see Chart 1).

These findings are borne out by the microscopical appearance. Though the gastric glands have begun to develop by the eighth week, differentiation of the cells first occurs at 16 weeks. At this age three types of cells can be clearly distinguished: (*a*) some containing mucin; (*b*) some large oval cells staining red with Biebrich scarlet and lying in the deeper parts of the glands, probably oxyntic cells; (*c*) smaller granular cells in the outer part of the glands, probably peptic cells.

Erepsin was present in extracts of the duodenal wall in 15 out of 22 cases, and was actually found in three out of five specimens of 16 weeks (see Chart 1). The sugar-hydrolysing enzymes were all present at birth, although inconstantly; invertase and maltase were also found at 24 weeks, but not previously (see Chart 2). We think that our failure to detect these ferments at earlier ages may be due to their relative instability. The presence of well-marked goblet cells in both villi and crypts at eight weeks suggests that mucin is probably present at this age, though tests for mucin were not actually made.

CHART 2.



Pancreas and Liver.

Pancreatic amylase was found in extract of pancreas in 13 out of 31 cases, the earliest at 22 weeks, but it is to be noted that it was not present constantly at full time (see Chart 2). Pancreatic lipase (20 cases) was found in 14 specimens, once at 32 weeks. Trypsin (17 cases) was present from 16 weeks, except in two specimens (22–23 weeks) (see Chart 1). The test for trypsinogen and enterokinase was not considered very satisfactory, and the results are therefore not included. Microscopically the islets were first detected at 75 mm. (10–11 weeks). By 12 weeks the islets were well differentiated, and the alveolar cells were strongly eosinophil and granular.

No chemical tests were carried out for the presence of bile-salts or mucin—i.e., the liver secretory products concerned in digestion. The anlage of the gall-bladder was seen in the 10 mm. embryo. Bile-ducts were first clearly seen at 12 weeks.

Discussion.

There are many difficulties in assessing the results of this investigation. There is, in the first place, little or no exact knowledge of the conditions present in the still-born fœtus effecting alteration or even destruction of bodies so unstable as enzymes, though it is known that certain factors are at work. For example, it is known that changes of hydrogen-ion concentration occur rapidly after death, and further,

[4] A large number of these tests were kindly carried out for us by Miss D. Woodman, M.Sc.

that these variations materially affect the activity of enzymes, but the exact influence of such changes on specific ferments is not known. Just as there are variations in the rate at which post-mortem changes occur in different organs, so also alterations of hydrogen-ion concentration and other post-mortem conditions may effect certain enzymes more rapidly than others, and thus it is probable that a negative finding is of less value than positive evidence.

Following up this line of argument, we submit that the carbohydrate-splitting ferments may be more unstable after death than the proteolytic enzymes, otherwise it is most remarkable that the latter are present as early as 16 weeks, whilst the former are not constantly found even at full time. In addition, contrary to expectation, there is very little correlation between the appearance of pancreatic amylase and intestinal maltase. Hydrochloric acid, though not present as early as pepsin, was fairly constantly found at birth. It is suggested in this connexion that both our own varied results and the inconstant findings of other workers may be due to post-mortem decomposition of the hydrochloric acid, or to vitiation of the Günzberg reaction owing to the presence of mucin.

Summary.

1. Proteolytic ferments present at 16 weeks. 2. Hydrochloric acid present at 19 weeks. 3. Rennin present at 19 weeks. 4. Pancreatic lipase present at 32 weeks. 5. Carbohydrate-splitting ferments found very rarely at 24 weeks and not constantly at full time. [No tests were carried out on material younger than 16 weeks.]

This research is part of a general inquiry into fœtal development, the expenses of which are being met in part by a grant from the Thomas Smythe Hughes Medical Research Fund.

Clinical and Laboratory Notes.

A NOTE ON BANISTERINE OR HARMINE.

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About a year ago Lewin [1] published results of an investigation of the actions of *Banisteria caapi* and of the alkaloid banisterine obtained from it. Extracts or decoctions of this plant have been used by natives of South America as a kind of intoxicant. From experiments on laboratory animals and on man, Lewin found that banisterine produced a stimulation of the central nervous system, followed, in the case of larger doses especially, by depression. On the basis of his experiments the alkaloid was tried in post-encephalitic rigidity with results said to be equal, or superior, to those obtained by the use of hyoscine in the same condition. At the end of this investigation Lewin was informed by Merck that the alkaloid banisterine was chemically identical with harmine. Both possess the same formula, $C_{13}H_{12}N_2O$. Lewin was able, from the literature on harmine, to adduce as points of agreement only the heightening of motor excitability up to convulsions, and stated that further experiments were necessary to establish the identity of banisterine and harmine.

At a recent meeting of the Berlin Medical Society, Lewin and Schuster [2] reported the results of the use of banisterine in cases especially of Parkinsonism. In the subsequent discussion Stern mentioned that he had employed harmine in a few cases with success, but Lewin did not admit the identity of action of harmine and banisterine. In a comment on the problem in THE LANCET it was stated that it is essential that a—

> "Pharmacological comparison of banisterine and harmine should be instituted as soon as possible. The point is important, because if Prof. Lewin's results are confirmed a demand may arise for this drug, and harmine can probably be made much more easily from the usual source, the seeds of *Peganum harmala*, than from the plant utilised by Prof. Lewin, *Banisteria caapi*."

Many years ago I carried out a somewhat detailed investigation of the pharmacological actions of the two alkaloids of *Peganum harmala*, harmaline and harmine. As the results of this investigation were published in the *Transactions* of the Royal Society of Edinburgh—a publication which is not usually searched for work of this kind—it is perhaps not surprising that neither Lewin nor anyone as far as I know, who has worked on banisterine or harmine, seems to be acquainted with my papers. As the result of data already to hand, it would seem possible to institute a comparison of banisterine and harmine from the pharmacological viewpoint; indeed, what difficulty there is arises from lack of detailed knowledge of the actions rather of banisterine than of harmine. As I have been investigating during the past year the actions of the nearly related tetrahydroharmine, in the course of which I have repeated many of the experiments with harmine and harmaline, I feel in a favourable position for making a comparison between the actions of banisterine and harmine upon the basis of such knowledge of the two alkaloids as is at present available.

The actions of the alkaloids of *Peganum harmala* were first investigated in 1895 by Tappeiner.[4] He gave a general account of the actions of harmaline—e.g., the motor stimulation of the central nervous system (tremors and convulsions), followed or accompanied by paresis; he described the slowing of the pulse, and he roughly estimated the lethality in laboratory animals. He also made a few experiments with harmine which acted very similarly. His investigation was stated to afford no basis for the therapeutic use of the alkaloids.

Some years later I described in greater detail the actions of harmaline [5] and harmine,[6] as a result of which I came to the conclusion that the actions of these alkaloids generally resemble those of quinine but that, in regard to the stimulation of the central nervous system, their actions resembled those of some of the other cinchona alkaloids rather than of quinine itself. On the basis of these experiments, harmaline and harmine were tried in malaria,[7] with the result that the former was found to have curative results in acute malaria, though inferior to quinine, but harmine gave promising, though (owing to the small number of cases available) not convincing, results in relapsing malaria. Flury [8] also investigated the actions of the harmala alkaloids, with very similar results so far as the nervous system and circulation were concerned.

In regard to my own position, further experience has confirmed my belief that there is a remarkable resemblance in their fundamental actions between the cinchona alkaloids and the harmala alkaloids. This is true, for example, of their actions on protozoa, on voluntary muscle, on the circulation, and on organs containing involuntary muscle—e.g., the uterus, spleen, intestine, blood-vessels. Unfortunately, no sufficiently detailed examination of such actions of banisterine has yet been done, but I should suggest to those who can obtain banisterine for investigation that if the latter possesses the following actions it would go far to establish the pharmacological identity of this alkaloid with harmine: produces contracture and inexcitability of frog's muscle in a concentration of 1 in 5000 or greater; contracts frog's blood-vessels; contracts the rabbit's uterus in concentrations of 1 in 20,000 or greater; relaxes the spleen and intestine; has a powerful toxic action on protozoa. If banisterine proves identical with harmine these actions will have to be kept in mind in its therapeutic employment.

In the absence, however, of detailed information of the pharmacological actions of banisterine, it is, I think, still possible to institute a useful comparison between the actions of the two alkaloids. In attempting to do this, I propose to direct special attention to their actions on the central nervous system, seeing that it is for this use that banisterine has so recently acquired its reputation.

It is in the first place interesting that both plants sources have been used to form a kind of intoxicant. Lewin has given an interesting account of this use of *Banisteria caapi*. I drew attention to the use of harmala seeds as an intoxicant in North Africa, with the comment [7]: "It is possible that in large doses it (harmine) will produce a kind of intoxication in man, seeing that it has been found to produce a pronounced stimulation of the cerebrum in the lower animals." Vertigo and nausea and slowing of the pulse are described as symptoms occurring in man with banisterine, and they occur also with the harmala alkaloids.

In laboratory animals, the action of the two alkaloids can be more easily compared. Lewin gives the minimal lethal dose of banisterine for guinea-pigs as 0·1 g. per kg., practically identical with what I found for harmine—viz., 0·12 g. per kg. In the rabbit he found banisterine caused death in a dose of 0·2 g. per kg. in 3–6 hours, while I found death from 0·23 g. per kg. of harmine in 2 hours 40 minutes. So far as lethality goes, the results are sufficiently near to allow the alkaloids being identical.

Lewin describes the symptoms produced in the rabbit by banisterine, and the closeness of the resemblance between that description and the effects of harmine in the rabbit as I described them is remarkable, as the following extracts will show.

Banisterine (Lewin).—Two minutes after injection the whole body trembled, the fore limbs were kept stretched in front. After seven minutes, short-lasting rotation movements round the long axis of the body followed. The animal lay down and made drum-beating movements with the fore limbs. (This was followed by a condition of stupor.)

Harmine (Gunn).—Five minutes after injection there were marked tremors of the head and fore part of the body and the hind limbs were extended so that the abdomen touched the ground. After 12 minutes a slight epileptiform convulsion occurred, after which the animal lay quiet. A similar but more violent convulsion occurred later during which the animal fell on its side and rolled over sideways two or three times. After this the rabbit lay on its side with feeble pawing movements of the limbs. (This was followed by a condition of motor paresis.) Considering that the dosage was different, the qualitative resemblance in the symptoms selected for mention is at least very striking.

No one could read the descriptions of the effects of the two alkaloids without being impressed by the resemblance. The chief symptoms produced by both are tremor and swaying of the body, with impulse to continual movement, especially "running" movements or "drum-beating" movements of the fore limbs. The tremor is aggravated by voluntary effort. With the related alkaloid harmaline I deduced from the symptoms the occurrence of hallucinations in cats, just as Lewin did with banisterine in dogs. So far as mammals are concerned it would seem impossible, on the present data available, to distinguish the actions of the alkaloids. Harmine produces slightly different symptoms in different species of mammals. A more exact comparison could be made by comparing parallel doses of the two alkaloids in different species of animals. The lethality of harmine for several species of animals has already been determined.[6]

The only apparent discrepancy is in regard to the frog. In a very brief account, Lewin describes a persistent heightened reflex excitability followed by paralysis of the extremities. The animal assumes a peculiar attitude in which the head is immovable as if in long-lasting opisthotonus, a posture which is not altered by death. On the other hand, I found no convulsive symptoms with harmine in frogs, but only paralysis of lower motor centres. Flury likewise found no convulsive symptoms with harmine. I did, however, point out the rigidity of the back muscles, ascribing it, I think rightly, to the local action of the injection into the dorsal lymph sac. I had found that solutions so low as 1 in 5000 produced rigid contracture of frog's voluntary muscles, and the hypodermic injection being much more concentrated very markedly produced this effect on the muscles of the back. Unfortunately no data are available in regard to the action of banisterine on frog's muscle. It appears to me, however, that Lewin may have confused such an action with a strychnine-like opisthotonus. Indeed, the fact that the posture was unaltered after death renders this local action almost certain.

Perhaps these points may suffice for the present to emphasise the extraordinary close resemblance between the pharmacological actions of banisterine and harmine. If the alkaloids prove to be identical, the fact does not of course detract from Lewin's initiative in being the first to employ banisterine in paralysis. Having exhausted my supply of harmine, I have not been able to try it in post-encephalitic conditions but I hope soon to have an opportunity of doing so. If harmine, whether identical with banisterine or not, proves of value in nervous diseases, the question will arise whether any of the allied alkaloids may not be even better. It is difficult to prophecy in view of the fact that the exact cause of the rigidity in Parkinsonism is not determined. If the beneficial effect is due to a stimulant action then harmine will possibly be superior to harmaline and possibly inferior to apoharmine. I hope to publish very soon a detailed account of the action of tetrahydroharmine.

References.

1. Lewin, L.: Arch. f. Exp. Path. u. Pharm., 1928, cxxix., 133; and Comp. rend. de l'Acad. de Sci., 1928, clxxxvi., 469.
2. Lewin, L., and Schuster, P.: See Deut. Med. Woch., March 8th, p. 419.
3. THE LANCET, March 9th, p. 537.
4. Tappeiner H.: Arch. f. Exp. Path. u. Pharm., 1895, xxxv., 69.
5. Gunn, J. A.: Trans. Roy. Soc. Edin., 1909, xlvii., 245.
6. Gunn: Ibid., 1911, xlviii., 83.
7. Gunn and Marshall, D. G.: Proc. Roy. Soc. Edin., 1920, xl., 140.
8. Flury, F.: Arch. f. Exp. Path. u. Pharm., 1911, lxiv., 105.

THE PRESERVATION OF ANÆSTHETIC ETHER.

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IT has been recognised for many years that anæsthetic ether, when stored, tends to oxidise and that peroxides, aldehydes, and other substances make their appearance. Furthermore, these decomposition products have been shown to be toxic and some even think that "ether convulsions" are due to their presence.[1] Organic chemists have done a great deal of work in trying to find means of checking this decomposition and their efforts have met with a large measure of success. In 1921 it was shown that carbon dioxide had a stabilising effect upon ether,[2] and many manufacturers both in this country and in the United States now treat their product in this way before it is bottled. Strong light and heat have also been shown to favour decomposition, and most ether is now put up in dark amber-coloured bottles with instructions for storing in a cool place.

Anticatalysts.

In spite of these precautions, however, ether still tends to oxidise when kept for prolonged periods, and efforts have been made to find a suitable anticatalyst which will inhibit this action. The addition of a small quantity of alcohol has been tried,[3] but this was not so successful as it was in the case of preserving chloroform. Metallic mercury has a slight but definite anticatalytic action, the most efficient form being that of "grey powder" which has a larger effective surface than the equivalent amount of metal in the

form of a globule. It has recently been shown, however, that copper is a most excellent anticatalyst and that ether stored in copper cans shows no tendency to decompose even in the most adverse circumstances.[4] It seems probable, therefore, that the storage problem is solved, and that in the near future ether will be put up in containers which are internally copper-plated.

The next difficulty to be overcome is the decomposition of ether through which gases are bubbled. At the present time many types of anæsthetic apparatus exist in which air, oxygen, or nitrous oxide and oxygen are passed over or through ether, and it is notorious that oxidation occurs very quickly under these conditions. Dr. C. F. Hadfield investigated the contents of the ether bottle of a sight-feed apparatus through which nitrous oxide and oxygen had been passed.[5] He found that decomposition varied with different ethers and was accelerated by heating the bottle. Furthermore, the figures for the aldehyde and peroxide contents showed marked correspondence. It occurred to me that it might be possible to utilise the anticatalytic property of copper already referred to, and thus inhibit the oxidation brought about by the passage of gases through ether.

Author's Experiments.

Accordingly, a polished copper plate about 8 cm. long and 3 cm. wide, giving an effective surface of about 48 sq. cm. was placed in the standard ether bottle of a Boyle's apparatus. Approximately one-third of the surface of the copper was above the ether level. This latter was kept fairly constant by the addition of fluid at frequent intervals. The ether used was the purest standard product obtainable, and nitrous oxide and oxygen in the proportion of 5 to 1 were bubbled through it for varying periods. The ether bottle was surrounded by a jacket containing water at room temperature and was exposed throughout to a strong artificial light. The experiments were then repeated without the copper plate and the various samples were analysed with the following results:—

Time of bubbling $N_2O + O_2$ in minutes.	Ether peroxide (parts per million).	
	Without copper.	*With* copper.
0 (control) ..	Less than 0·05	
30	2·5	1·2
60	2·2	0·2
90	1·0	0·5
	Aldehyde (parts per million).	
0 (control) ..	1·0	
30	9·5	2·5
60	11·5	2·5
90	4·0	1·5

This appeared to show that a copper plate does materially diminish oxidation, and it was next decided to find out whether the actual tube which dipped into the ether could be made of copper and produce similar effects. A copper sheath 5 cm. long was therefore made and fitted over the end of the bubbling tube. On repeating the analyses, however, it was found that the rate of oxidation was not changed from that of a standard control. This negative result was thought to be due to an insufficient area of copper above the ether level and another tube 9 cm. long was made giving a total effective surface of about 56 sq. cm., of which about one-third was above the ether level. The series of experiments was then repeated, the analyses reading as follow:—

Time of bubbling $N_2O + O_2$ in minutes.	Ether peroxide.	Aldehyde.
	Parts per million.	
0 (control) ..	0·05	1·5
30	0·05	2·0
60	0·05	5·0
90	0·05	5·0

These results show that practically no oxidation had occurred and that the previous supposition was correct in that an adequate surface of copper must be present above the ether level to secure the best results.

In studying these analyses it may be noticed that in some cases the amount of impurities found after 90 minutes passage of gases is less than that after 60 minutes. This curious result was also observed in the similar but much slower oxidation which occurs with stored ether.[4] It is found that ether kept for two years usually contains less aldehyde and peroxide than that stored for only six months. The probable explanation is that further decomposition takes place and that traces of organic acids are left as the end-product of the reaction.

Conclusions.

1. Pure ether treated with carbon dioxide and stored in copper containers will keep pure almost indefinitely.

2. If anæsthetic gases are bubbled through ether for prolonged periods the rate of decomposition will be greatly diminished if there is an adequate area of copper above and below the ether level.

My thanks are due to Mr. F. H. Carr, F.I.C., who arranged for the chemical part of this investigation to be carried out at the British Drug Houses Analytical Laboratories.

References.—1. Wilson, S. R.: The LANCET, 1927, i., 1117. 2. Wallis, R. L. Mackenzie: THE LANCET, 1921, i., 1173. 3. Finnemore, H.: Proc. Roy. Soc. Med., March, 1924. 4. Nitardy, F. W., and Tapley, N. W.: Brit. Jour. Anæsth., 1928, vi., 53. 5. Hadfield, C. F.: Proc. Roy. Soc. Med., 1928, xxi., 1699.

NOTE ON THE INHIBITORY EFFECT OF A STAPHYLOCOCCUS ANTIVIRUS IN RELATION TO THE pH OF THE MEDIUM.

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Louros and Gaessler (*Klin. Woch.*, 1927, vi., 1662) have stated that the inhibitory effect of a streptococcus antivirus is due merely to the development of acidity in the medium. They found that the filtered broth culture of a streptococcus had a hydrogen-ion concentration corresponding to a pH of 5·0 to 5·8, and point out that streptococci cannot in any case live in this medium because of its high acidity. Further, they found that streptococci would grow in the filtered broth as soon as it was neutralised with a phosphate buffer solution. They therefore question the existence of a streptococcus antivirus. The following experiment shows that the conclusions of Louros and Gaessler do not hold in the case of a staphylococcus antivirus.

A 500 c.cm. flask of ordinary peptone broth, standarised colorimetrically to a pH of 7·8, was inoculated with a mixed culture of eight strains of staphylococci which had been isolated from the pus of various lesions. The flask was incubated at 37° C. for 36 days. The culture was then filtered through a Berkefeld filter and the filtrate was reinoculated with the same mixed culture of staphylococci and incubated at 37° C. Slight initial growth occurred, but it did not increase macroscopically after 48 hours. The incubation was continued for 17 days, and the culture was then filtered through a Berkefeld filter. The pH of the filtrate was determined electrometrically and found to be 8·6 (two determinations).

To 10 c.cm. of sterile filtrate was added one loopful of pus from which staphylococci had previously been isolated. No trace of growth occurred. In a control broth, similarly inoculated with pus, there was abundant growth of staphylococci.

Further experiments have shown that final sterilisation of the filtrate by steam on three successive days has no effect either on the hydrogen-ion concentration or on the inhibitory power of the filtrate. In one such experiment the pH of the heat-sterilised filtrate was found to be 8·1. Ten cubic centimetres of this filtrate when inoculated with one loopful of a young mixed culture of staphylococci showed only a trace of initial growth, which ceased after 24 hours' incubation.

It is evident, therefore, that the inhibitory effect of a filtered broth culture of staphylococci is not due to the development of acidity in the medium.

Medical Societies.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES.

AT a meeting of this Society on April 5th Dr. F. J. COUTTS, the President, took the chair and a discussion on

VENEREAL DISEASE IN THE MERCANTILE MARINE

was opened by Dr. H. M. HANSCHELL. His experience, he said, had left with him the deep impression that the seafarer, sailing in and out of the Port of London, was anxious to secure expert medical advice and treatment for his venereal disease, and without loss of time. In the sailor these diseases differed in no particular from those of the landsman. The latter had attended in considerable numbers at the clinic which he had had charge of for ten years, and therefore he was in a position to make comparisons. He had had under care for these diseases about 7000 male patients of every nationality, creed, and shade of colour. The recently noted decrease in the incidence of primary and secondary syphilis applied to both seamen and landsmen. More than half the white seafaring men patients he saw acquired their infection in England, and for the most part in London. Most of them got it from prostitutes whom they paid, as also did the majority infected at ports abroad. An increasing proportion of men, he found, sought advice because they feared an unhappy result from their last coitus; of 700 white seamen so attending 124 were found not to have venereal disease. The ages of the infected seamen he saw ranged from 18 to 27. In his last 700 consecutive white cases 10 were infected in North America, 32 in Australasia, 52 in South America, 83 in the Far East. Liverpool figures would probably show different proportions. Of the last 900 consecutive seamen he had seen, 200 were either Asiatics or negroes. Venereal diseases were carried from country to country far more by passengers than by those who worked the ships, and it was not so easy for the latter to hide their disease. Examination of passengers had not yet been extended to include the genitalia, but crews for ships in British ports had to pass a medical examination before they could sign on for another voyage. The majority of seamen in this country were so examined two or three times a year. Stewardesses were medically examined, but not their genitalia. Doubtful cases found during the ordinary medical examination were sent to the clinic, but many of these turned out not to be venereal disease, and though there had been delay in reaching the diagnosis so that a man lost his chance of signing on a ship, no complaint was made. The man was given a certificate to this effect, and this absolved him from a further examination. Dr. Hanschell suggested that some such close working connexion between the venereal diseases clinic and the medical examination of the crews before signing on was necessary; the clinic should be near where the signing on took place, and should not be restricted as to hours. Sometimes disease became manifest on the voyage though it had not been detected at the medical examination.

There was considerable variation, said Dr. Hanschell, in the equipment and capacity of ships' surgeons. Some had not had any first-hand experience in the modern technique of diagnosis and treatment of venereal disease, and comparatively few ships carried proper irrigation apparatus, or such drugs as salvarsan and bismuth. This was a reflection of the neglect of adequate teaching on the subject in the medical schools, but improvement in this respect was now evident, and it was not so seldom that patients came to the clinic armed with careful notes of their case. He believed that most steamship lines had a waiting-list of applications for the post of surgeon, and it would be easy to insist that applicants should produce evidence of capacity to diagnose and treat these diseases by modern methods. Clinics had had an educative effect on even lay members of the crew, and when no surgeon was on board it was clear that treatment was conducted on sound lines. When on shore the men did not delay in seeking advice. Seamen suffering from these diseases did not wish to go home; they asked to be treated at hospital. And they were becoming more fastidiously conscious of their responsibility for the spread of venereal disease. He pleaded for a better education of ships' surgeons in this matter, and more modern and adequate equipment. The great aim should be to prevent cases of venereal disease going on board ship.

Dr. A. O. ROSS (Liverpool) drew a vivid picture of the relaxations awaiting the returning seaman at the ports, conspicuous among which were the opportunities, especially when in drink, of promiscuous sexual congress. Few seamen, he found, continued the treatment until they were cured; some were even too lazy to read the instructions. Institutes existed at Liverpool which catered for the men's amusement and many efforts were made on their behalf. He criticised the poor accommodation for the crews on many ships, even important ones, remarking that several foreign countries set Britain a good example in this regard. He had come to the conclusion that until there was better discipline and the men were provided with more generous accommodation on board ship a serious incidence of venereal disease would continue. In a large series of cases Dr. Ross said his proportions for the different venereal diseases worked out as follows: gonorrhœa, 61 per cent.; syphilis, 29 per cent.; chancroid, 10 per cent. He added that 15 per cent. of the patients at his seamen's clinic were Liverpool townspeople, who found it more convenient to go there than to attend clinics nearer home. South American ports he stigmatised as plague spots in regard to venereal disease, the cases coming from them grossly exceeding (taking into consideration the tonnage concerned) those from any other part of the world. On the other hand, he had high praise for the efficiency of the treatment carried out at Singapore. Of 3000 cases in his clinic 18 per cent. were foreign. Acute cases he persuaded to sign off their ship. Chronic cases were allowed to sail again under promise to renew treatment on their return. For gonorrhœa he thought adequate treatment could only be assured with certainty ashore. Many seafaring men did not regard this disease with any particular seriousness; some indeed were contemptuous about it.

Discussion.

Dr. H. WANSEY BAYLY said most seafarers were of the virile type, who would not be dissuaded from satisfying their sexual instinct, hence prevention should be concentrated upon by giving instructions as to cleanliness and disinfection when risk had been encountered. Measures of this kind in certain ships of the Navy had proved most effectual.

Dr. M. T. MORGAN spoke of the work of a committee of the Board of Trade in the direction of revising the scales of drugs and medical appliances to be carried by various classes of ships. Similar attention had been paid to the medical guide for captains whose ships did not carry a surgeon; and the next subject to which the committee would direct its attention would be the scales for ships carrying a surgeon.

Mr. J. F. PEART referred to the great value of the treatment of gonorrhœa by argyrol.

Dr. JOHN ADAMS spoke of the rarity of cases of chancroid in London nowadays as compared with 40 years ago. He considered that very often surgeons on board ship were inadequately trained for dealing with cases of venereal disease, and insufficiently equipped. There should be a more thorough training of medical men attending clinics for instruction; they should actually do the injections under expert supervision, in order to gain confidence.

Colonel L. W. HARRISON said that the papers by Dr. Hanschell and Dr. Ross, as also remarks by Dr. Adams, confirmed the opinion which he had held for a long time that the regular treatment of a man of the mercantile marine suffering from venereal disease could be secured only by his remaining ashore. It seemed rather hard that a seaman should have to remain ashore so long, and he thought the remedy lay not only in ships being better equipped in material for the modern treatment of venereal disease, but in ships' doctors being better trained to use this equipment. Whatever might be thought about the practicability of continuing afloat treatment commenced ashore, there was no escaping the necessity of accurate diagnosis and skilled treatment of men whose disease began on the voyage. His own experience led him to believe that this was by no means always satisfactory, and he could endorse what had been said about the frequency with which sores had been treated with lotio nigra, or other antiseptics, before microscopical diagnosis had been made. He was particularly glad, therefore, to support Dr. Hanschell's suggestion to take advantage of the numbers of candidates for the post of ship's doctor by insisting on these previously undergoing a post-graduate course of instruction in the modern diagnosis and treatment of venereal disease.

Mr. JONES (National Union of Seamen) and Rev. Mr. DEMPSEY (British Sailors Society) urged the need of prevention, and spoke of the provision being made to entertain the men when they came ashore. Mr. Dempsey thought that one of the greatest assets on the part of the medical man encountering these cases was the adoption of that kindly attitude towards the sufferer.

Commander CAVILL (R.N.R.) praised the efforts being made by various societies on behalf of seamen, and said a real need was the education of the public, land as well as seafaring, to the seriousness of these diseases.

The PRESIDENT agreed that centres for the treatment of seamen ought to be quite near the docks, otherwise the proportion coming for treatment would not be satisfactory. Apparently some of the clinics were so well and considerately conducted that the men attended faithfully. He feared there was much truth in the contention that the only way in which to treat sailors in an effective way was to treat them ashore; but he would not like to think that would be so in the future, as he hoped that when the man went back to sea he would be able still to have proper treatment. He hoped a firm stand would be made in the way of ensuring that doctors appointed to ships should be qualified to treat these diseases properly, and have the equipment which would enable them to do this.

Mrs. NEVILLE ROLFE asked what medical provision could be made for the large number of men engaged in the coastwise trade of the country and those in fishing fleets. Both these classes of men were a long time from home and were in the way of acquiring disease in consequence, and she asked how their treatment needs could be at present met in such places as Fowey and Lowestoft. She also asked whether difficulty was experienced in inducing British seamen to go to foreign clinics for treatment.

Dr. HANSCHELL, in the course of his reply, said he did not think the classes of men mentioned by Mrs. Rolfe (in which he included men working the Thames Estuary) received treatment at all. Yet, if the disease were diphtheria instead of syphilis, hospital accommodation would be quickly found for them.

Dr. ROSS also replied. He agreed that the coastwise men were badly treated in regard to venereal disease. There did not seem to be a V.D. clinic for seamen at Bremen, but cases there were passed on by the British Consul to a practitioner who made the necessary injections at a trifling charge beyond the cost of the drugs.

ROYAL SOCIETY OF MEDICINE.

WAR SECTION.

A MEETING of this Section was held on April 8th, with Lieut.-General Sir MATTHEW FELL, the President, in the chair, to discuss

FUNCTIONAL NERVOUS DISORDERS IN THE SERVICES.

Colonel J. C. KENNEDY said the discussion originated in the fact or belief that during the last few years the incidence of hysteria in the Army had been increasing. It was not surprising that many men should have broken down under the strain of their war experiences, but under normal circumstances hysteria was not looked upon as of much importance among disorders of the male. He was sure, however, that in this time of peace, hysteria existed to a quite appreciable extent. In the five years before the war cases of disease of the nervous system were estimated at 5·7 per 1000 strength, in which the figure for hysteria was 0·1, neurasthenia 0·6, and epilepsy 0·9. In 1927, on the other hand, nervous cases amounted to 7·5 per 1000, with hysteria 0·7, neurasthenia 1·4, epilepsy 0·9. Colonel Kennedy analysed 177 cases occurring during the 18 months following Jan. 1st, 1927. In a few the diagnosis was uncertain, the reasons being: (1) that clinical details were lacking, and so the cases had to be excluded; (2) that the men were suspected of malingering; or (3) that there was some associated condition, such as high blood pressure or duodenal ulcer, or a possibility of organic nervous disease such as encephalitis lethargica or disseminated sclerosis. No case should be diagnosed as hysterical when the symptoms were associated with the presence of an organic abnormality. The 154 cases left, out of the 177, when doubtful ones had been excluded, were grouped according to the main clinical symptoms: (*a*) those in which fits or convulsions were the main symptom, of which there were 82; (*b*) those in which tremors or spasms were predominant, 10; (*c*) those presenting paralyses, disturbances of sensation, and aphonia, 19; (*d*) those with mental symptoms (including amnesia) predominating, 43. Patients in the first group were admitted to hospital for observation of a fit, which might be simply an attack of vertigo, a fainting attack, or an epileptiform seizure. There was a high incidence of these cases in the first two years of service, showing that there had probably been some inherent defect in the person. Young adults during a first experience of a hot climate, if subjected to physical or mental stress, especially if associated with over-indulgence in alcohol, might throw epileptiform fits which were indistinguishable from those of true epilepsy. In group (*b*) tremor and spasm, a history of nervous disability in youth or before enlistment was pronounced. In group (*c*) Colonel Kennedy had noted the power of suggestion, several cases of aphonia having occurred in series. The mental group (*d*) constituted nearly one-third of the total number. The illness was characterised by great irritability and loss of self-control, episodic attacks of delirium or frenzy, and exaltation and depression. Somnambulism, hallucinations, double personality, amnesia, and craving for sympathy were also seen. It was not uncommon to get a history of uncontrollable temper, and in two cases chorea had occurred early in life. There was much evidence that the basic factor in hysteria was a constitutional or inherent instability of the nervous system. These cases afforded ample illustration of Babinski's contention that hysteria was the outcome of suggestion, and that it could be cured by counter-suggestion and persuasion. The manner of disposal of the patients was recorded in 151 instances: 113 men were returned to duty and 38 were found unfit for military service. A large proportion of the invalids manifested mental symptoms.

It might not be easy, Colonel Kennedy continued, to differentiate hysteria from malingering, or from organic nervous disease; still more difficult was it to

decide whether one was dealing with a reflex nervous disorder, such as might be associated with a wound. Hysteria might be superimposed upon an organic lesion, or upon a toxic condition. In the "Nomenclature of Diseases" of the Royal College of Physicians, which the Army adopted, no name was provided intermediate between neurasthenia and psychasthenia; hence it was difficult to place such psychoneuroses as anxiety, compulsion, and obsessional neuroses. Some of the cases diagnosed as hysteria and included in group (*d*) could be more accurately described as anxiety neuroses. As to the disposal of cases of hysteria, he thought the decision whether a hysterical patient should be retained in the Service or not depended on a collective consideration of the length of service, the evidence of previous history, and the effect of treatment. In cases in which hysterical symptoms developed soon after enlistment and there was a definite previous history of nervous disability, the patient could be of but little use in the Service. The treatment, apart from general considerations of health and the application of electrotherapy, took the form of counter-suggestion or persuasion. A patient who was not easily amenable to persuasion might require a prolonged course of treatment and ceased to be an economical proposition for the Army in peace time. Still, the principle that no man should be discharged from the Service uncured of a curable disability was one which he would like to see carried out. The question of specialist psychotherapeutic treatment was receiving attention. The situation was different in war time, when the whole of the resources of the country were devoted to the maintenance of man-power. The problem remained, in essence, one of eugenics and upbringing.

Rear-Admiral E. T. MEAGHER said he was excluding from his discussion occupational neuroses, such as writer's cramp, chorea which might arise as a result of psychic shock, and exophthalmic goitre. People fell into three groups—normal, psychopathic, and neuropathic. Some held that there was a germinal defect, and that the majority of people who subsequently developed mental defect or disorder had this deficiency. A terrifying shock might have a more or less permanent effect on the mind of a child, but unless neuropathic or psychopathic, such a person was not likely to develop a psychoneurosis. He did not know any way of determining whether such inherent weakness existed in a particular individual. He thought a new entrant to the Service should be under observation in the first months to see whether he manifested any characteristics indicating nervous instability. It was agreed that, apart from hereditary predisposition, a normal person if subjected to exceptional stress might break down. Conditions in the Navy tended to raise the resistance to hysteria. Hysterical manifestations could often be traced to some psychic shock. In the Navy the hysterical fit was common, and for these cases a word or two of advice and discharge to duty was the best course to adopt. Hysteria was manifested most in the less educated; indeed, he had not seen a case of pure hysteria in an officer. It was easily provoked in those of neuropathic constitution.

In regard to diagnosis, the chief thing was to make sure that organic disease did not coexist. According to Kraepelin, 50 per cent. of cases of manic-depressive insanity showed hysteria. In treatment the medical officer should adopt measures to check loss of emotional control by advice or by isolating the patient. Galvanism would cure aphonia, and the hysterical fit could be cut short by physical measures. The doctor must gain domination over the patient. It had been found that the "Old Contemptibles" were not liable to displays of functional nervous disorder. The Navy did not show much change in the incidence of functional nervous disease as compared with the years before the late war. In conclusion, the speaker advocated uniformity of nomenclature and terminology for all the Services and for general use.

Squadron-Leader M. L. BURTON said the problems in the Royal Air Force differed somewhat from those in the Army and the Navy, for in peace time the stresses in flying were more pronounced than in those other branches. Even the more stable type of man might break down if the stress was exceptional. The highest figures for the incidence of functional nerve disease in the Air Force were in 1922–23; since then there had been a steady decrease. The incidence was highest among those actually flying; those who through age or other cause did not fly regularly came off best. In neurasthenia the predominant symptom was mental or physical fatigue, with pains, headaches, digestive disturbance, with general depression and lack of energy. In the anxiety neurosis the symptoms were mainly psychic, and the picture was one of nervousness, the patient had a sense of foreboding, worried over trifles, and was easily disturbed. Psychasthenia was characterised by a defective power of volition; the patient was unable to make and act on decisions; doubting mania also occurred, and claustrophobia. Only a small number of flying officers broke down, even when subjected to exceptional stress. Psychoneurosis developed because the subject could not adapt himself to his environmental condition. Some cases of functional nervous disorder occurred after mild head injury, which might have been so slight that concussion was not suspected. When a toxic factor had been operative the case would usually respond to appropriate treatment.

Dr. ALDREN TURNER spoke of what had been found in officers at the War Office Medical Board. These cases were usually of a special character. Hysteria, as illustrated by the usual stigmata of paralysis, fits, and anæsthesia, was rare. In young officers there had been cases of fits developing under special circumstances of mental strain and over-work, and perhaps to some extent aggravated by personal habits and climatic conditions, as in India, and in these cases the fits usually ceased on the return of the patient to this country. The outstanding functional nervous disorder observed among officers was neurasthenia, using that term in its widest application. For the purposes of description he had made three groups: (1) the more purely debilitated or nervously exhausted cases; (2) those showing evidence of anxiety, accompanied by characteristic physical signs; (3) those with the post-concussional syndrome. In the group characterised by anxiety, causes of a psychological kind played an important part, including distaste for certain duties and disciplines. Thyroid enlargement in these cases was practically unknown, but there was reason to believe there was a disturbance of endocrine function and of the vegetative nervous system. Those who suffered a breakdown during the war were thereby rendered liable to a relapse if strain and stress were renewed.

BRITISH PSYCHOLOGICAL SOCIETY.

The Psychiatric Section of this Society held a joint meeting with the Psychiatry Section of the Royal Society of Medicine on April 9th. The chair was taken by Dr. EDWARD GLOVER, President of the former section. A discussion on

THE PSYCHOPATHOLOGY OF ANXIETY

was opened by Dr. ERNEST JONES. He said that the term "morbid anxiety" distinguished a collection of phenomena from those grouped under the name of "fear." Two features justifying this distinction were disproportion between the stimulus and the response, and disharmony between bodily and mental manifestations. In pronounced cases, such as claustrophobia in a closed room, these were very marked, but in borderline instances it was difficult to assess "normal" distress. Psycho-analysts had learned to set a very high standard of "normal" bravery, and to maintain that much timidity passing as normal was really neurotic and curable. The anxiety nature of the physical manifestations was often overlooked clinically. Symptoms such as chronic diarrhœa, psychical

impotence, sweating, and flatulent dyspepsia were often wrongly interpreted. Bodily manifestations were much more striking in morbid anxiety than in normal fear, and suggested a thwarted instinct. Another well-recognised feature was the internal disharmony among the manifestations themselves. The physical groups did not seem to be constituted for any biological purpose. Mentally there was neither activity nor passivity, but a curious mixture of over-excitation with paralysis. Physically the dissociation might go so far as to produce a mainly mono-symptomatic picture. These features strongly suggested a disorder rather than a simple exaggeration of the fear instinct.

The Freudian View of Anxiety.

Freud had, primarily on a physical basis, separated morbid anxiety from the "neurasthenia" group of Hecker and had regarded it as due to undue sexual excitation with deficient opportunity for discharge. The anxiety was found in place of frustrated libido, and the physiological basis was generated from the physiological basis of libido by some unknown process of chemical transformation. Phobias presented the same picture of anxiety appearing as substitute for a thwarted libidinal impulse. Morbid anxiety was a perverted manifestation of the fear instinct which, in neurotic conflicts, had been stimulated to activity as a protection against the threatening libido. It was the ego's fear of the unconscious. Real dread (i.e., fear of real danger) concerned the ego only and had nothing to do with the desires of repressed libido; it was a normal protective mechanism. Nevertheless real dread contained one useless element which closely resembled morbid anxiety. On the affective side there was a state of anxious preparedness and watchfulness, a useful state but useless when—as often—it passed over into terror, which paralysed both body and mind. Even in situations of real danger a state of developed dread was not part of the useful biological mechanism of defence, but an abnormal response akin to the neurotic symptom. Freud had suggested that this developed dread was derived from the narcissistic libido attached to the ego. The anxiety of war shock and probably also that of hypochondria developed in four stages: (1) perception of external danger; (2) normal fear-response of mental alertness and physical preparedness; (3) over-investment of the ego with narcissistic libido as a protective response; and (4) evocation of morbid anxiety on the part of the ego to the excess of narcissistic libido. The last stage was useless and indeed detrimental as far as the external danger was concerned. Obviously uncontrolled libido could be a danger to the ego; there were manifest social risks and unconscious infantile fears were at work. In face of the infantile situation the child had been helpless, alarmed, and at the end of its resources, and its erotic wishes had been impossible to gratify. To the infant strong excitation without relief was tantamount to losing the very capacity for obtaining relief; the most familiar clinical manifestation of this state was the castration complex. The first step in the child's attempt to cope with this state of affairs was the group of reactions later to be called morbid anxiety. The apparent lack of purpose and coördination reminded the observer of the earliest reactions of the infant to distress, and they performed certain functions. Some of them, notably the over-activity of excretory organs, furnished a limited gratification and relieved tension. Others—for example, the respiratory manifestations—called attention to the urgent need for help. In more extreme states a protective paralysis occurred, and the last resort of the child, as of the neurotic, was an artificial inhibition of vital activity, including the disturbing impulses. Freud—and before him Erasmus Darwin—had suggested that many characteristic features of anxiety were copied or even derived from the event of birth. Only careful correlation of the phenomena of birth and of morbid anxiety with the various manifestations of the fear instinct in animals would give final light on the puzzling problem of the relation between external and internal danger, of the conflict between the interests of the individual organism, and the threat provided by the activity of racial impulses.

Anxiety in the Psychoses.

Dr. HENRY YELLOWLEES suggested that Freud meant a totally different thing by "anxiety" from the meaning applied to the term by psychiatrists. Text-books of psychiatry allowed no place to anxiety among the psychoses save in involutional melancholia, in which it almost invariably played a part. Craig and Beaton called agitated melancholia the "associated psychosis" of anxiety. Clinical observation showed that the true psychoses had little or nothing to do with Freud's anxiety state. Freud had described generally increased nervous instability, whereas the true psychotic was remarkably indifferent to stimuli like noise. The anxious patient imagined the worst in any given set of circumstances, and exaggerated possibilities, but no extension of this mechanism would ever produce the delusions of the melancholic, who ignored possibilities. The melancholic, if he could escape for a moment from his delusions, dealt efficiently with real emergencies; the speaker had known a melancholic doctor, who spent his time banging his head against the wall, turn and deal effectively and professionally with a fellow-patient who had an epileptic fit. There was no better aid to differential diagnosis than an air-raid. Freud had spoken of vertigo, digestive disturbances, particularly ravenous hunger, paræsthesia, and phobias as characteristic of the anxiety state; these were not features of melancholia.

Discussion.

Dr. BERNARD HART said that the theory of transference of libido into anxiety was quite intelligible chemically but not as part of a psychological and biological concept. He agreed with Dr. Jones that fear was an integral part of the reaction to danger and that anxiety and dread were identical in their essential mechanism—in both the ego was failing to master the situation—with the one important difference that anxiety was the response to internal stress and real fear or dread to external danger. The essence of the reaction was not so much the protection of the ego as the failure to protect it adequately. Dr. Rickman had spoken in this connexion of the "helpless ego." If the response to external danger were completely reactive there was no fear, and if the response to internal stress were completely reactive there was no anxiety. If dread was not a part of the normal reaction to danger some other factor was required to account for it, but whatever this factor might be it must afflict a very large proportion of the human race, for dread was extremely common. "Ideal" or "fully adaptive" would be a better phrase than "normal." Other exciting causes than narcissistic libido would fit in with the failure of the ego to master danger. In war-neurosis there was anxiety as long as the struggle to keep unpleasant memories out of consciousness was only partially successful; anxiety disappeared when a fairly adequate pathological adaptation–amnesia, existed or when the situation was altered by treatment and the relation of the ego and the partial memories was adjusted. The full picture of anxiety neurosis did not appear in true psychoses because the clinical picture was modified by the peculiarities of the psychosis, but the chief characteristics of morbid anxiety, if defined as apprehension, tension, and unrest, were clearly discernible in psychoses, especially in involutional melancholia and alcoholic psychosis. The other factors mentioned by Dr. Yellowlees were secondary and derivative. Ravenous hunger was certainly not typical of anxiety.

Dr. R. D. GILLESPIE said that certain well-known states of mental unpleasure arose from conflict, but he doubted whether repression or morbid sexual history were essential factors. One form of anxiety was associated with cardiac lesions. It was obviously

protective, but there was some evidence that frustrated instincts might produce a number of states, not anxiety alone. He questioned whether the new-born child showed signs of anxiety, though of course it might have shown them before the final "knock-out" of birth. Obstruction of breathing in a young baby produced signs not of anxiety, but of anger. Shakespeare had anticipated both Erasmus Darwin and Freud, when he ascribed the fearlessness of Macduff to the fact that he had been born by Cæsarean section.

Dr. J. A. HADFIELD said that there were difficulties in the way of ascribing anxiety states to physiological disorders. Patients might suffer and die from severe toxic conditions without manifesting anxiety; others might appear in normal health and vigour and yet have terrible dreads. Although toxic foci might be found in most cases of anxiety it was likely that they would also be found, if sought, in most normal people. A morbid fear might come on in a 'bus and not in a tube or taxi; were we therefore to believe that the toxic condition became active only in Regent-street and not in Leicester-square? Anxiety might often be dispelled by suggestion, but it was hard to see how the toxicity was cured in this way. There was an intimate connexion between adrenalin and anxiety, but to prove this relationship causal it must be shown that injection of adrenalin produced anxiety. He agreed with Dr. Jones that emphasis should be laid on the psychological factor; that anxiety was abnormal under any circumstances, and that it was not a transformation of libido into fear, but he differed in regarding anxiety as due to fear in the ordinary sense and not only to threats to the libido. It often might be due to threats to the sexual libido, as in nightmares, but conflict between egoistic aggressiveness and fear of obliteration was a common cause. Some marked cause of fear in infantile life very constantly turned up in analysis, and might be regarded as a factor predisposing to the attack of fear. Anxiety states were infantile reactions and fear was one of the most constant experiences of childhood. The infant reacted by fear to noise and to the withdrawal of support, and the older child reacted to fear by egoism and amenableness. Any threat to these precipitated anxiety in later life.

Sir MAURICE CRAIG pointed out that no disorder consisted of one symptom and that anxiety appeared in many conditions. From the therapeutic standpoint he wanted to know why these factors became effective. Pavlov's work held out a hope that something might be done to prevent their operation.

Dr. W. H. STODDART said that for a long time he had been unable to differentiate between involutional melancholia and the melancholia of manic-depressive insanity because anxiety occurred in both. He had found anxiety states also in paranoia, but did not agree that they were characteristic of all neurosis; some obsessional cases might show no anxiety. He believed the value of potassium bromide to lie in its anaphrodisiac properties.

Dr. WILLIAM BROWN pointed out that one-seventh of all men invalided from the army were victims of neurasthenia, despite the fact that 70 per cent. of those who came to special shell-shock centres were fit to be sent back into the line after treatment. He therefore agreed with Dr. Hart in requiring explicit evidence of narcissism as the cause of the neurosis, which must be very common. Fear was the result of failure of adaptation and was distinct from the instinct of self-preservation. He protested against the use of the term "libido" as if it were something that could be repressed and had its own energy.

Dr. L. S. KUBIE asked whether an anxiety situation would always lead to an anxiety state. The hysteric might have no emotional content, although the origin of his condition lay in a difficult emotional situation often tinged with anxiety. The absence of anxiety from the picture of psychotics still left the problem of what part anxiety might have played in the production of their symptomatology.

Dr. T. A. ROSS described a case in which anxiety was manifested without any lack of direct sexual expression. The psycho-analyst might claim that this expression had been absent in early childhood, but the childhood of the patient had offered several far more obvious causes of fear; he had lived in fear of hell inculcated by a religious father and of destitution because his parents were in the habit of leaving him alone in the evenings. Sex differences were to be found everywhere, but these other difficulties were extremely important. The whole life of many children was one of discomfort and fear.

Dr. JONES, in reply, agreed that by "normal" he meant "ideal" or "completely adapted," which was very rare indeed. The total figure for shell-shock in the army only worked out at about 2 per cent., which was the figure also given for homosexuality among the general population. He agreed that anxiety might be due to conflict in respect of hatred or aggressiveness, but held that the vast bulk of those emotions were evoked as a result of thwarted libidinal impulses. Why was a patient afraid of his libido? Obviously because of what it might lead to, and murder was one of the most likely things.

Dr. YELLOWLEES also replied.

EDINBURGH OBSTETRICAL SOCIETY.

AT a meeting of this Society on March 15th, with Dr. HAIG FERGUSON, the President, in the chair, a paper on

A SCHEME OF MATERNITY SERVICE

coördinating antenatal, domiciliary, and hospital treatment was read by Dr. JAMES YOUNG. It was now generally agreed, he said, that the high maternal mortality and morbidity rates were dependent primarily on the inadequacy of the machinery of present-day midwifery. The present service by medical men was wasteful of lives and health because the duties of general practice were incompatible with satisfactory midwifery. The annual death-rate amongst mothers in England and Wales was about 5 per 1000 live births. This implied the death of about 3000 women every year and, on a moderate estimate, at least 30,000 more women annually suffered more or less lasting damage from childbearing and childbirth. The best results were found where the service was carried out by midwives with doctors available for the emergencies. The proved advantages of such a combine were seen in the practice of the Queen Victoria Jubilee Institute for Nurses of England and Wales and in the outdoor practice of the large maternity hospitals, where the death-rate was very low. An ideal practice in these respects was the East End Maternity Hospital in London, where for many years the death-rate in a total of about 2000 unselected cases treated annually was under 1 in 1000—that is, about one-fifth of that obtaining over the rest of the community. On analysis the reason for the low death-rate in these hospital practices was found in the fact that they were carried out by self-contained units, each serving its own district, in which the normal cases were conducted physiologically by midwives and in which the antenatal supervision and the management of the abnormal cases were carried out by the doctors belonging to the service. In this way there was a continuity of supervision and control of the antenatal, the domiciliary, and the hospital treatment of the patients and of the personnel responsible for the services. The system made for a physiological management of the 90 per cent. or thereabouts of normal cases and for early discovery and efficient treatment of abnormalities.

Dr. Young believed that an adequate maternity service was possible only if planned on a national basis, having as its object a coördination of the activities of the midwife, the doctor, the National Health Insurance, and the local authorities, which at

present were unrelated and often overlapped. This service should work in conjunction with voluntary agencies, such as hospitals, and should include: (1) a midwife for every labouring woman; (2) antenatal supervision of every case; (3) a service by doctors for complications; and (4) the hospital. Pending establishment of a national service much might be done if local authorities undertook to make provision for their own needs. It was important to relieve doctors in busy general practice of the duties of midwifery, and the doctor personnel or the service should consist largely of general practitioners selected because of their special experience and training and of a comparatively small number of specialists. Dr. Young believed that in every area the "unit" system should be aimed at as far as possible for, by ensuring continuity of treatment and responsibility, it would lead reciprocally on the one hand to an elevation in the standard of domiciliary practice and on the other to a prevention of the tragedies of the present-day maternity hospitals. The fact that all cases were under the control of the unit from the beginning meant that there was no vitiation of the hospital environment by the introduction of women with passages infected before admission by the injudicious management of some outside attendant over whose methods the hospital had no control. In this way the atmosphere of the hospital was kept secure for clean midwifery. In the East End Maternity Hospital in London, whose practice was based on this sytem, sepsis had been practically eliminated for many years. On the other hand, infection of the normal case was one of the outstanding disadvantages of the present-day maternity hospitals, which opened their doors to clean and unclean alike. The recent report of the Scottish Board of Health on maternal mortality referred to the high death-rate in maternity institutions in Aberdeen due to this contagion and other writers (for example, Dame Janet Campbell) had referred to the same thing. In the Edinburgh Royal Maternity Hospital there had been 72 cases of puerperal sepsis with five deaths amongst normal spontaneous deliveries in four years. Dr. Young spoke of the complexity of the segregation problems which faced every such mixed hospital and raised the question whether, under the present unsatisfactory conditions of maternity practice, it might not be desirable to abolish the large mixed hospital and, in such districts, to have two kinds of hospital, the one for "booked" and clean cases—that is, those under the supervision of the hospital—and the other for the infected or suspect cases. He believed that the "suspect" case (for example, the unsuccessful forceps case, the case of placenta prævia plugged before admission, and the abortion) raised even greater segregation difficulties than the frankly septic case and that the tragedies of the hospital sprang chiefly from it.

Dr. E. FARQUHAR MURRAY (Newcastle) read a complementary paper on

The Future of Obstetrics,

with Special Reference to the Development of a Maternity Service. The main criticism of the present system, he said, was that essential services were not available for many patients of the industrial classes, and he indexed the essential requirements as: (1) Antenatal supervision. (2) Clean surroundings during the confinement which takes place under the supervision of a midwife. Also an abundance of surgical dressings and lotions. (3) A doctor who is on call to assist delivery, to repair lacerations, and to deal with complications. (4) Good nursing. (5) Postnatal supervision. (6) A consultant service. It was absolutely essential that the nursing should be good, and this would never be obtained so long as "handy-women" were tolerated. A maternity nursing service should be organised under direct medical supervision and control, and trained nursing should be placed at the disposal of a doctor whose patient was unable to make provision for it. Such a nursing service under the supervision of a sister midwife would ensure that accurate temperature charts were kept, and the onset of inflammatory processes would be recognised early. The nurse would report the presence of fever to the sister midwife who would at once inform the doctor. The present system of allowing the midwife full charge was fundamentally wrong, and would never be righted until there was properly organised medical supervision of this nursing. Dressings should be available for even the poorest patients, and such dressings would consist of an accouchement sheet, wool, binder, diapers, and towels. The dressings would be sterilised and the nurse would be responsible for those which should be returned. Antenatal centres should be established and should be available for all doctors engaged in industrial practices. The antenatal centre should be staffed by the general practitioner who resided in the area and not by whole-time officers or specialists.

The organised maternity service should work somewhat as follows. Each woman would select a doctor and would enter her name at the nursing centre. The doctor would carry out the antenatal examinations. Nursing service would be responsible for the routine urine examination and health visits. The doctor would be called to the confinement if required by the midwife, and certain routine visits would be paid during the puerperium. Consultant services should be available for any cases of difficult labour with which the practitioner could not deal. An emergency service should also be organised which would provide at short notice a nurse, blankets, hot water-bottles, transfusion apparatus, and, if necessary, a specialist. By this means, instead of transferring a shocked and collapsed patient to hospital the specialist and nurse would be rushed to the patient. The cost of this scheme could be met without making any demands on the State or the approved societies as the maternity benefit could be used for its administration.

ERRATUM.—Mr. N. Howard Mummery writes: "May I correct certain errors in the report of my paper recently read at the Royal Society of Medicine's Dermatological Meeting and reported in your issue of March 30th. I stated that the chief aim of an industrial medical officer was to prevent the occurrence of dermatoses. I did not state, as I am reported as saying, that, in the main, private or panel medical practitioners, or factory surgeons, had an inadequate knowledge of dermatoses. I said that they had an inadequate knowledge of the conditions of employment and of the home conditions of industrial workers. Further, I am made to say that I rejected for employment persons 'showing marks of seborrhoic states': this phrase should read 'showing marked seborrhoic skin states.'"

BRITISH ORTHOPÆDIC ASSOCIATION.—The Robert Jones Medal and Association Prize for 1928 has been awarded to Mr. E. P. Brockman for his essay on Club Foot (Congenital Talipes Equinovarus).

BRITISH EMPIRE CANCER CAMPAIGN.—The quarterly meeting of the Grand Council of this Campaign was held on April 8th, with Lord Reading in the chair. The following grants to London institutions were made: £3500 to the Cancer Research Department of the Middlesex Hospital, £650 for research at St. Mark's Hospital, £80 for research by Dr. J. C. Mottram at the Radium Institute, and a sum of £500 for special investigations to be made at the Cancer Hospital under a scheme submitted by Dr. E. L. Kennaway.

The newly formed Cancer Research Centre in the North of Ireland was invited to become an affiliated body of the Campaign. The Council extended its congratulations to the recently organised New Zealand Branch of the Campaign, which was inaugurated during a visit to Wellington by Mr. Sampson Handley.

The summary of the recommendations made by the Committee of the International Conference on Cancer held in London last July, was submitted to the Council, which passed on the recommendations to the Investigation Committee of the Campaign. Inter alia the Committee strongly urges that the British Empire Cancer Campaign, in collaboration with the Medical Research Council and the Ministry of Health, should invite all institutions using radium and X rays to utilise an agreed form of record.

Reviews and Notices of Books.

Colour and Colour Theories.

By Christine Ladd-Franklin. London: Kegan Paul, Trench, Trübner and Co., Ltd. 1929. Pp. 287. 12*s.* 6*d.*

There are three main theories of colour sensation. The first is the Young-Helmholtz theory, the basis of which is physical, founded on the proved fact that all the colours of nature can be imitated by three selected spectral colours in appropriate proportions. The second is that of Hering, the basis of which is chemical. It postulates a retinal mechanism which permits the alternate composition and decomposition of three different chemical substances by the action of light, giving rise to six different colour sensations, among which are included black and white. The third, that of Edridge-Green, is evolutionary, and shifts the mechanism for the distinguishing of colours from the retina to the brain, those individuals who are more highly developed in this respect being capable of distinguishing a greater number of colours than those who are less developed. Dr. Christine Ladd-Franklin, who is a psychologist, declares her main objection to the Young-Helmholtz theory to be that though the sensation white may be produced by a mixture of red, green, and blue lights, white is nevertheless not a red-green-blue sensation. We are asked to believe, she says, that when we experience the sensation of a faint colourless light we are really sensing red and green and blue without knowing it, and this idea, she says, is so bizarre that it would seem as if to mention it were enough to show its inadequacy. Dr. Ladd-Franklin's own theory, being a chemical one, approaches more nearly to that of Hering, but, she says, the fact that red and green must be regarded as a colour pair which, when combined, result in white, is fatal to Hering's theory; the combination actually produces yellow. Her own theory she terms the "molecular dissociation theory." The retinal basis of the light sense is a photochemical process, and the eye which furnishes the colour sense contains more complicated chemical substances than do the retinæ, which are defective. She supposes a chemical substance which under the influence of light undergoes dissociation, but whereas in the rods (which do not convey any colour sensation) this dissociation is at once complete, in the cones the process is more complicated and takes place in successive stages. In a primitive evolutionary condition, and also in the totally colour-blind individual, the cone process is absent—i.e., there is no partial dissociation and no colour sensation. In a more advanced condition the partial dissociation of the colour molecule gives rise to the colour sensations yellow and blue, a state of things which exists not only in the partially colour-blind, but also in the more peripheral parts of the retina where the cones are sparse, and also in twilight. A further dissociation of the molecules which give rise to the yellow sensation, or some of them, occurs in the normal individual, giving rise to two new sorts of molecules which excite the sensations red and green respectively.

The theory is both chemical and evolutionary, and in the latter respect has something in common with that of Edridge-Green, but whereas the latter regards the evolutionary process as cerebral, Dr. Ladd-Franklin looks for it in the chemistry of the retina. It is remarkable that although there is a detailed discussion in this book of the two older theories, that of Edridge-Green is entirely ignored. Certainly in one respect Dr. Ladd-Franklin's theory has the advantage, in that it is not inconsistent with monocular colour blindness, a condition which, though very rare, has occasionally been discovered. It is a pity that this book is not more systematically written. It consists in fact of reprints of a number of essays which have appeared in various periodicals from 1892 to 1927, so that there is a great deal of repetition without much logical sequence. At any rate, however, it provides material which cannot be ignored.

Neurosurgery.

Principles, Diagnosis and Treatment. By William Sharpe, M.D., Professor of Neurosurgery, New York Polyclinic Hospital and Post-Graduate Medical School; and Norman Sharpe, M.D., Attending Neuro-surgeon, St. Mark's Hospital, New York. London: J. B. Lippincott Company. 1928. Pp. 762. £2 2*s.*

Few comprehensive works on neurological surgery have appeared in recent years, though during that time the specialty has been one of the most active branches of surgery. The appearance of this rather expensive volume will therefore be hailed with interest; but the reader who hopes to find an accurate and orderly description of the more recent developments of neurological surgery will suffer disappointment. The book is an account of the authors' personal experience and consists for the most part of *ex cathedra* and oft-repeated statements of their somewhat heterodox views. Thus, undeterred by the experiences of the Great War, the authors advocate early laminectomy ("after the patient has rallied from the initial shock of the injury") for spinal injuries producing compression of the spinal cord. They also favour laminectomy in certain types of multiple sclerosis. For gliomas of the brain they prefer simple decompression to removal of the tumour and they are very pessimistic as to the outlook in these cases, though it has for some time been known that many gliomas possess a very low degree of malignancy and operation in these may be followed by freedom from symptoms for a number of years.

The first part of the book is devoted to surgical conditions of the brain. After a comparatively short chapter on tumours, brain abscess is discussed in an interesting way. The authors put forward a view which is unusual, but perhaps not unreasonable, when they urge that subtemporal decompression should be performed in most cases of temporo-sphenoidal abscess and that exploration of the brain for the abscess should take place through the subtemporal incision and not through the infected field of the mastoid operation. In the chapter on head injuries a short account is given of personal work on injuries at birth. The authors found from lumbar puncture in a series of some 500 newly born infants that intracranial hæmorrhage of varying degree occurred in 9 per cent. of the cases, particularly in first-born full-term males. They suggest that in these cases the early institution of repeated lumbar punctures will prevent the onset of cerebral spastic paralysis. Hydrocephalus, cranial deformities, the methods of neurological investigation and of cranial operations are discussed in turn. In subsequent sections, the surgery of the spinal cord, cranial nerves, and peripheral nerves is considered. There is also a chapter on the surgical treatment of early selected cases of purulent meningitis, in which the main point taken up by the authors is that in cases of localised purulent meningitis, associated with disease of the mastoid process, subtemporal decompression should be performed on the corresponding side of the head.

It will be readily gathered that the authors hold original ideas about neurological treatment and their book certainly stimulates the reader to reconsider the basis of many existing beliefs. They would have strengthened their work greatly if they had paid more attention to the orthodox views of the period and had introduced their points of controversy with detailed case reports and complete statistical information of their personal experience. Such cases as have been reported for the most part do not support the authors' arguments, or are so lacking in essential details that they arouse in the reader the suspicion that the book has been too hurriedly prepared.

X RAY EXAMINATION OF THE HEART.

Radiologia Clinica del Cuore e dei Grossi Vasi. By CESARE PEZZI, Professor of Medical Pathology, University of Milan. Milan: Cooperativa Farmaceuta. 1928. Pp. 334. Lire 40.

THE technique of X ray examination of the heart and great vessels has been greatly developed and perfected during recent years, and at the present time the X ray method must be considered as valuable as the electrocardiograph, if not more so, in the investigation of cardiovascular disease. Not only can the actual size of the heart be determined from the teleradiogram or orthodiagram, but valuable information is also obtained from a study of the contour of the heart and aorta viewed from different angles, and of the character of the pulsation.

Prof. Pezzi, in a monograph dedicated appropriately to Vaquez and Bordet, has given us a comprehensive account of the application of X rays to the study of the heart. He prefers orthodiagraphy to teleradiography as the most serviceable method of recording the exact size and shape of the organ, and he advocates the rather complicated system of measuring the orthodiagram elaborated by Vaquez and Bordet. After describing the technique employed, and the normal appearance and dimensions of the heart shadow, he discusses the modifications seen in disease, valvular lesions, heart failure, pericardial effusion and adhesions, hypertension, angina, and less common affections all being considered in detail. Three chapters are devoted to the aorta in health and disease, and here the illustrative radiograms are particularly good. On the subject of congenital malformations and of affections of the pulmonary artery Prof. Pezzi is a recognised authority, and the X ray appearances in these conditions are fully described. Expansile pulsation of the pulmonary arteries in the lung roots—the so-called hilum dance—is regarded as diagnostic of pulmonary incompetence. The text is profusely illustrated throughout by anatomical figures, orthodiagrams, and radiograms, and an adequate bibliography is given at the end of the book.

The treatise is likely to become a standard work on the increasingly important subject of the X ray examination of the heart.

THE SETTING OF FRACTURES UNDER THE FLUOROSCOPE.

La réduction des fractures sous écran radioscopique. By Dr. RADUTZESCO, formerly a Foreign Assistant in the Surgical Therapeutic Clinic of the Faculty of Paris of Dr. Pierre Duval; Surgeon to the Hospital "Regina Elisabeta" in Bucharest. Preface by M. PIERRE DUVAL. With 125 figures in the text and on 48 plates. Paris: Masson et Cie. 1928. Pp. 196. Fr.50.

Dr. Radutzesco in this small monograph describes and advocates a method of setting fractures, especially those of the lower end of the forearm and of the leg, with the help of the X rays and fluoroscopic screen. He sets forth the advantages of this method both in the reduction of the displaced bones in their fixation in plaster, and subsequently in examinations carried out to make sure that the correction and fixation remain satisfactory. He warns his readers against the dangers of frequent exposure to the rays and gives details of the precautions necessary to minimise the quantity of exposure. The special form of fluorescent screen used consists simply of an oblong screen, the "pelle radioscopique du Dr. Henri Béclère," measuring 13 × 18 cm., to which is attached a long handle set in a plane parallel to but above that of the fluorescent surface. Its obvious resemblance to a spade has suggested its name. The fluorescent material is covered by a piece of lead glass 10 mm. thick. Full details and a series of radiographs are given of seven cases of fracture near the wrist, one of the shaft of the humerus, and four of the ankle. Inhalation anæsthesia is recommended for the setting of fractures of the upper extremity and spinal anæsthesia for the lower. The results, immediate and remote, appear to have been excellent. Dr. Radutzesco points out that there are pitfalls awaiting the unwary in the application of this method, and he tells readers how to avoid them. The same methods might no doubt be used in fractures of other parts of the limbs, but less easily and less completely than in those of the wrist and ankle. They seem to us to be too elaborate to be practicable in the rush and hurry of a general hospital. In private work a surgeon with the necessary time, experience, and apparatus at his disposal may hope to secure excellent results with fracture treatment in this way.

GROWTH.

By W. J. ROBBINS, S. BRODY, A. G. HOGAN, C. M. JACKSON, and C. W. GREENE. New Haven: Yale University Press. 1928. Pp. 189. With 83 figures. 14*s.*

THESE five semi-popular lectures by members of the staff of the University of Missouri deal with the nature of growth, its statistical, nutritional, and morphological aspects, and the influence of the ductless glands. The most interesting perhaps is Prof. Brody's summary analysis of the course of growth and senescence, which deals with facts that ought to be familiar to anyone concerned with nutrition. Though when he gets away from facts, and says—e.g., "Why does growth occur? Because there is an inherent tendency which causes cells to divide," we could wish he had put a footnote "this is a joke" or "this is not a joke," as the case may be. The other four chapters are all good, and we can heartily recommend the book as an introduction to a great subject.

THE DIFFERENTIAL DIAGNOSIS OF BLOOD DISEASES.

Praktische Differentialdiagnostick. Teil 8. Blutkrankheiten. By Dr. ALBERT HERZ, Lecturer at Vienna University. Dresden: Theodor Steinkopff. Pp. 86. M.8.

THIS slender volume, containing less than a hundred pages, is a surprisingly complete synopsis of modern knowledge of blood diseases. It contains little that is new, but omits little that is important. The arrangement is logical, and reference is easy: but illustrations are scanty and poor, and technical details are inadequate and scattered through the text. It is, however, a satisfactory work for the purpose for which it was written, and many clinicians will probably find that this reasonably priced book will give an answer to the everyday problems of differential blood counts.

BACTERIOLOGY.

Morphologic Variation and the Rate of Growth of Bacteria. By A. T. HENRICI, Professor of Bacteriology in the University of Minnesota. London: Baillière, Tindall and Cox. 1928. Pp. 194. With 36 figures. 13*s.* 6*d.*

THE early ideas about the abundant pleomorphism of bacteria were completely upset by the discovery of adequate methods of making pure cultures. In the rebound there has been a long period in which bacteria have been thought to be much more uniform in size and shape than they really are. Prof. Henrici has been looking again at the forms of several species and measuring them at different stages of growth under various conditions, and he has made out that they change in accordance with plans which can be approximately ascertained. Some, at any rate, of the pleomorphism which has lately been supposed to represent life-cycles can be explained along these simpler lines; though the author does not deny the possibility of complicated modes of reproduction, he merely says they are not proven.

LE CANCER PRIMITIF DU POUMON.

Étude anatomo-clinique. By RENÉ HUGUENIN, Ancien Interne Lauréat des Hôpitaux de Paris; Préparateur du Laboratoire d'Anatomie Pathologique de la Faculté. Paris: Masson et Cie. 1928. Pp. 330. Fr.50.

THIS monograph appears at an opportune time. Lung tumours have been prominently under the notice of clinicians and pathologists during the last ten years, and although much has been written on the subject the information is scattered. A comprehensive and complete study such as Dr. Huguenin has made is therefore of particular value. The work has involved deep research into the literature as well as an intimate study of many cases which have come under the personal notice of the author. All aspects are treated exhaustively. Our ideas of the pathology of cancer of the lung at the present time are undergoing some revision, especially in regard to the nature and origin of the oat-cell tumours, and Dr. Huguenin shows a critical appreciation of the problems at issue. The question of ætiology, too, he approaches with caution. In the clinical section, and especially in that part concerned with diagnosis, some original observations have emerged from personal experience of the author and his colleagues. A large section of the book is concerned with descriptive notes of 46 cases of chest tumour. The histological drawings and skiagrams illustrating lung cancers are excellent. The monograph will doubtless take its place as a standard work on tumours of the lung and mediastinum.

WHITHER MANKIND.

A Panorama of Modern Civilisation. By 18 contributors. Edited by C. A. BEARD. London: Longmans, Green and Co., Ltd. 1928. Pp. 408. 12*s.* 6*d.*

THIS book is based on "the assumption that science and the machine are two invincible facts with which all must reckon. Those who refuse to face them are condemned in advance to sterility and defeat." It consists of 18 essays under the titles, Science, Business, Labour, Health, Religion, the Family, Play, and so forth, in which the respective authors speculate on where we are and where we shall be. It is, in short, yet another symposium on the spirits of the age and, as generally happens, the authors immensely overrate the importance of their catchwords and forget the spirit of the ages, of which any philosophical biologist could have told them; curiously enough there is no such collaborator in the list.

FROM THE SEEN TO THE UNSEEN.

By JOHN H. BEST, B.Sc. Lond., Vicar of Little Marlow, Bucks. London: Messrs. Longmans, Green and Co., Ltd. 1929. Pp. 552. 18*s.*

THIS is an attempt, well documented and supported by much scientific and philosophic knowledge, to prove that there is an existing God, Who, in the words of the Prayer Book, is the "Maker of heaven and earth, and of all things visible and invisible." Such being the proposition, its demonstration is proceeded with in an orderly manner. A preliminary section having discussed the chief characteristics of life, animal and vegetable, and the relations existing between plants and animals having been demonstrated, the doctrine of evolution is found not to militate against any of the arguments that can be adduced for belief in a Divine design. The following two sections deal with physiology and embryology on recognised lines, the summaries which close the sections being clear and instructive, and proving the author to have followed carefully the lessons of much reading and to have real skill in presenting those lessons briefly. Up to this point the author has been attempting to show, especially in the passages closing each section, that every attempt to arrive at the sufficient cause of embryonic development along purely mechanistic lines is doomed to failure. Now, in a section discussing memory and instinct, he emphasises the fact that the manner in which our memories are preserved strikes at the root of any theory which would explain the universe only in terms of chemical and physical forces. A section on astronomy and the possibilities of human life or life in any form on other planets brings us to a long concluding section in which the great ethical and religious situations now placed before the reader are discussed, together with the arguments for a belief in the hereafter.

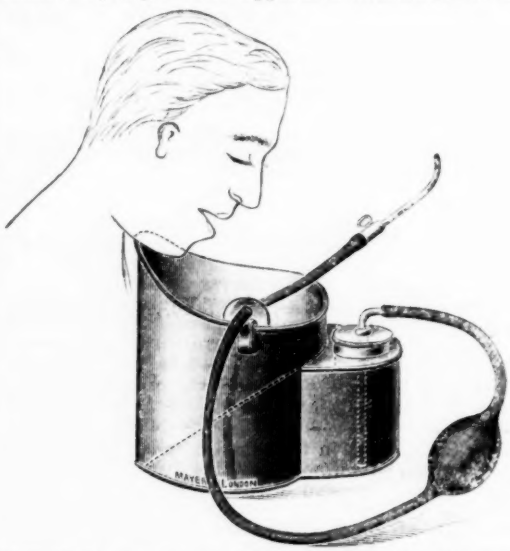
If there is no hereafter, the author pleads as the result of his arguments, not only will the evolutionary process to all intents and purposes have run its course in vain, but in vain will have been all men's efforts to bring their wills into harmony with God's through obedience to those higher impulsions which He Himself has put within them. The difficulties lying ahead of any writer who attempts to answer the fundamental questions involved in such an inquiry are familiar to everyone, and readers will judge for themselves whether the author's arguments establish what he so ardently hopes to be true. But his attempt to re-enforce faith in religion and to abate scepticism by reasoned argument is worthy of great praise for the labour expounded.

New Inventions.

A LAVAGE APPLIANCE.

MAINLY FOR THE ACCESSORY NASAL SINUSES.

UNLESS a gravity douche can is used the lavage of the accessory sinuses implies the holding by the patient, the nurse, and the surgeon between them two more or less clumsy vessels, the lotion holder and the receiver, both of which usually slop over, and a detached syringe. The apparatus illustrated is an



attempt to overcome all these difficulties by combining the two chambers in one appliance. The can is held by the patient and the surgeon or nurse has both hands free to control the cannula and the syringe, which is securely held by its detachable fastener to the can. An assistant is not required and, if necessary, the patient, by placing the can on a table, is able to carry out the lavage unaided and in comparative comfort. The clip on the Higginson syringe is detachable.

The apparatus (which is shown disproportionately large) could be used equally well for eyes, ears, or any other part of the body, and in almost any position.

This model has been made for me by Messrs. Mayer and Phelps.

HUGH E. JONES, L.R.C.P. Lond., M.R.C.S. Eng.

THE LANCET.

LONDON: SATURDAY, APRIL 13, 1929.

ON THE PASSING OF MUCH WATER.

POLYURIA is a symptom met with in many conditions, varying from the heightened nervous tension associated with (say) a medical examination for life assurance, when it appears in transient form, to the continued passage of large quantities of urine in serious states such as diabetes insipidus and chronic disease of the kidney. In his Goulstonian lectures, whose publication is complete in our present issue, Prof. E. B. VERNEY has attempted to interpret the pathological polyuria of these two conditions in terms of the findings and theories of experimental physiology. It has long been known that the polyuria of diabetes insipidus can be controlled by the subcutaneous injection of an extract of the posterior lobe of the pituitary gland, and the natural conclusion has been drawn that the symptom is due essentially to some interference with the function of that body. But clinical observation has shown that destruction by disease of the whole hypophysis is not necessarily followed by diabetes insipidus, while the results of experimental extirpation of the gland have been conflicting. The view, therefore, has been advanced that the polyuria is due to a disturbance of the hypothalamus, leading to a failure of this part of the brain to regulate the output of water and chloride by the kidney, and is not directly due to a lack of pituitary secretion. In a series of ingenious experiments Prof. VERNEY demonstrates how the gradually increasing polyuria which develops when the isolated kidney is perfused in a heart-lung preparation can be inhibited in a remarkable fashion, not only by adding pituitary extract to the circulating fluid but also by perfusion with the blood passing through the head and neck of another animal. He further shows that when the pituitary body is removed from this animal polyuria is re-established. From these and other experiments he concludes that the polyurias associated with diabetes insipidus, with water ingestion, and with isolation of the kidney, have an immediate ætiology common to all—viz., a decline in the amount of antidiuretic hormone normally secreted by the pituitary gland into the circulating blood stream. And he puts forward the interesting speculation that in the development of vertebrate animals upwards from the fish and amphibian, the demand for an increased control over the salt-and-water metabolism of the body has been met by a corresponding change in the function of the pituitary gland.

In his second lecture Prof. VERNEY examines from a new angle ROSE BRADFORD'S fundamental observations on the effects of reducing by surgical means the amount of kidney tissue in the dog. ROSE BRADFORD had shown that after the removal of even a small amount of the kidney it was exceptional for the urine to return to its original quantity and density, the most usual result being a distinct increase in the urinary water. By perfusing in parallel two kidneys in the isolated state, Prof. VERNEY and his colleagues found that the functional removal of half of one kidney by tying a primary branch of the renal artery, resulted in an immediate and similar polyuria from that organ. It was found, further, that the chloride excretion was increased relatively or even absolutely, but that there was a profound fall in both the percentage and absolute amounts of urea eliminated. The reduced kidney, in fact, responded at constant blood pressure exactly as though it were being subjected to an increase in perfusion pressure. What is the precise mechanism culminating in this response is not clear, but from the conditions of the experiment it obviously must be a strictly local one. On the basis of these experiments and the results of recent work on the physiology of the kidney, the lecturer seeks to explain the well-known series of events in chronic nephritis—the early disappearance of the rapid swings in the rate of urine eliminated by the healthy kidney during the daytime, the increase in volume passed during the night, the slight variation in the earlier stages from the normal in the water excretion, urea concentration, and chloride concentration tests with little or no rise in blood pressure, followed by increasing loss of kidney function, persistent rise of blood pressure and, finally, death from renal failure. He assumes that some toxin applied continuously or discontinuously to the glomerular vasculature leads to a gradual diminution in the efficiency of the renal units. Each must work longer to fulfil its function (of maintaining the constancy of composition of the "milieu interne") with the result that there is first a reduction in the normal periods of quiescence, and later increased activity night as well as day. The death of some of the units leads to the development of a greater pressure stimulus on the others with resulting secretion of a more copious urine which approaches the plasma in its composition. In time this intrinsically developed pressure is not sufficient, and a higher general blood pressure is demanded to increase the circulation through the kidney. This sustained rise in blood pressure is contributed to, Prof. VERNEY thinks, by a change in the activity of the vasomotor centre, resulting either reflexly from the kidney or from the presence in the circulation of abnormal substances.

The Goulstonian lectures are, in fact, full of highly interesting speculations, but the lecturer wisely asks, how are all these mechanisms correlated and integrated in the struggle to preserve the composition of the body fluids at their optimum? That question, as Prof. VERNEY remarks, is as yet unanswered.

PUBLIC CLEANSING IN GREATER LONDON.

SOME three years ago a deputation from the London County Council urged upon the Minister of Health the need for investigation of the means taken in London for the disposal of house or other refuse. The Council had received complaints of the nuisance caused to their new housing estate at Becontree by the large dumps of refuse at South Hornchurch, which had been accumulating for more than 50 years. These dumps, in some places 90 feet high, are used chiefly for the deposit of house and trade refuse from the cities of London and Westminster, the annual increment being in the neighbourhood of 350,000 tons, an amount probably in excess of that collected annually in Manchester. Although at the start these dumps were remote from a populated area, and more or less unnoticed, they now present a huge disfiguring mass, the peculiar smell from which is said to reach the southern part of the Becontree Housing Estate; they are frequently on fire, and the cloud of smoke may reach the houses now being erected within the urban district of Hornchurch. These and all the large uncovered riverside dumps are extensive fly-breeding grounds; the amount of rat infestation is

also very great. They pollute the surface water in the large shallow pools as well as the open drainage channels in the marshland. Authorities of other areas outside London, chiefly in West Middlesex, where smaller editions of the Hornchurch dumps are found, have protested against their districts being made dumping grounds for refuse from other areas. Nuisance, however, is not inevitable with dumping. At Northolt, for example, where frequent complaints were made a few years ago, there has been little, if any, objection raised since direct labour has been employed and the principle has been adopted of dumping in shallow layers and covering the fresh refuse with suitable innocuous material. In Hertfordshire and Bedfordshire, where great quantities of London refuse are dumped, complaints have been forestalled and conditions greatly improved as the result of careful management on the lines of the tipping precautions laid down by the Ministry of Health.

In his recent report[1] to the Ministry, Mr. J. C. DAWES takes the view that the present system of barging to dumps is open to criticism, especially as there is little effective competition between the contractors concerned, who have no regard for sanitary principles. The mounds created in the course of brick-making are a case in point. Hundreds of millions of so-called stock bricks are made every year, especially in the vicinity of Sittingbourne, with the aid of London household refuse; "fine ashes" or dust must be added to the virgin earth, "cinder" or breeze being commonly the only fuel used in the clamps to burn the brick. The brick-making industry appears capable of utilising some 700 of the 3000 to 5000 tons of refuse produced daily in London. Many brick-makers consider that household refuse should be allowed to stand before use; the fine ash content is thereby increased, possibly by the breaking down of the organic matter in which it is lying or to which it is attached, and from which in the fresh state it cannot be separated. But during this period of maturing a nuisance is produced which, unfortunately, cannot be met by covering with soil. Mr. DAWES suggests the making of a technical investigation by the industry to determine the possibility of using only separated ashes and breeze, holding out the inducement that these two items may cost them less than the crude refuse.

The magnitude of the problem is clearly seen from Mr. DAWES's report. In the years 1925–26, the collection of 1,130,000 tons of London house refuse and 72,000 tons of trade refuse cost the huge sum of £660,460, or 11*s.* per ton; its disposal required another £448,809, at the rate of 7*s.* 6*d.* a ton; and, in addition, street cleansing cost £1,086,118. The main gist of the report is that expenditure could be reduced by the formation of a central cleansing body for Greater London, to undertake both collection and disposal. Such a procedure has its precedent in the Metropolitan Water Board, and in the arrangements, less complete it is true, for the common disposal of sewage from the metropolitan boroughs and some of the areas adjoining London. The pooling of water-supply or sewage disposal was simplified by the fact that most, if not all, of the component factors of these problems had long been known and, to some extent, worked out. In the collection of house refuse, although the requisites are known—for it is obvious that the refuse must be stored on premises in a sanitary manner, and the material collected by methods which avoid the scattering of dust—we have by no means reached any final solution, although those responsible for the work in London and its vicinity have been active in their search. Experimental work is being done on the methods of collection, the best receptacle used, and the mode of its storage on premises, the most suitable type of dust collecting vehicle; on the disposal side, improved methods of dealing with tips have been devised and employed, improvements have been made in the construction of dust incinerators and in the utilisation of the constituents of refuse, both before and after incineration. Seeing that London represents almost the largest conglomeration of dwellings and premises in the world, and the difficulties bear some proportion to the size of the area concerned, the measure of success already achieved is gratifying. But any committee appointed to consider the question of giving effect to the report will be confronted with difficulties owing to the absence of accurate data. No doubt by the extended exercise of existing powers a reduction could be made in the cost of collection, caused by overlapping of refuse collection and street cleansing services; on boundary roads between boroughs, for instance, refuse is collected and the roads are cleansed at the present time by different local authorities. Section 140 of the Metropolis Management Act, 1855, enables the London County Council to order that any street or line of street, which is in more than one borough, shall be placed under the exclusive management of one of the borough councils for such purposes as cleansing. The difficulties and expense of accurate costing will militate against the committee's obtaining reliable evidence as to the further possibility of reducing by any appreciable amount the cost of collection; in fact, it would seem probable that the adoption of methods of collection tending to increase its amenities will increase the cost. In the absence of suggestions for improvement of the best known methods of disposal at present available and already in force, it is difficult to see what can be done beyond recommending the extended adoption of these methods. In the near future it should be feasible to mitigate the nuisance caused by incineration plants, and it is not too much to hope that the attempts to use crude refuse as a fuel to produce steam for the generation of electricity will be better rewarded. When a measure of success has been obtained in both these directions it is possible that certain geographical combinations of London might bring about the extended use of inoffensive incinerators helping in the supply of electricity. A proposition more ready for application at the present time would be concerted action to reclaim by dumping the low-lying marshland on the banks of the Thames, incidentally a means of providing unskilled work for the unemployed.

[1] Public Cleansing, being a Report of an Investigation into the Public Cleansing Service in the Administrative County of London. By J. C. Dawes, O.B.E., M.I.Mech.E., Inspector of Public Cleansing, &c., Ministry of Health, H.M. Stationery Office, 1*5s.*

CANCER OF THE LUNG.

AN important contribution to the study of cancer of the lung has lately been made by Dr. GEORGIANA BONSER,[1] who has compiled a statistical record of all the cases of intrathoracic tumour reported in the post-mortem room of the Leeds General Infirmary during the last 37 years. Her work is of special importance because her figures, unlike most of their kind, afford no evidence of an increase in the incidence of these tumours in recent years. The average percentage for the 37 years was 1·06, the highest figure, 1·30 per cent., occurring in the period 1908–12. This question of an increase in the incidence of intrathoracic tumours, a considerable proportion of which

[1] Jour. of Hygiene, 1929, xxviii., 340.

appear to be carcinomas of the bronchi, naturally interests cancer workers because it is surmised that air pollution may play a part in the ætiology of the condition. It has undoubtedly seemed to many pathologists, both in Europe and in America, that this form of growth is seen in the post-mortem room relatively more often than formerly, and in most places the figures, when analysed, have shown that this is indeed the case. Nevertheless it is fully appreciated that fluctuations in post-mortem room statistics may depend more on selection of suitable cases for demonstration purposes than on the actual incidence of the disease in the population. In Leeds this factor has not played a great part because, as Dr. BONSER points out, over 83 per cent. of all persons dying in the hospital during the last 37 years have been examined at autopsy. This is certainly an unusually high percentage for a hospital in this country and it makes her findings all the more significant. In 1927 J. B. DUGUID [2] collected the cases from the post-mortem records of the last 60 years in the Manchester Royal Infirmary, and there it was found that the incidence was unusually high—on an average more than twice as high as that in Leeds—and that it was steadily on the increase. Since Manchester is especially notorious in respect of atmospheric pollution, comparison of the figures with those of other less industrial towns was expected to furnish some information about the relation of this form of new growth to the degree of contamination of the air. It is perhaps fortunate for the advancement of medical science that the first comparison was made by Dr. BONSER in Leeds, for the atmospheric conditions in that city are so far comparable with those of Manchester as to render the Leeds figures more suitable as a control to the Manchester ones than as a contrast to them. At all events the difference in the incidence of the tumours in the two towns was far greater than the difference in their atmospheric conditions, and factors other than air pollution must be considered as influencing the figures. Dr. BONSER further demonstrates how complicated is the problem by showing that although the incidence in the post-mortem room at Leeds has not increased, the percentage incidence in the wards of the hospital has shown a definite rise since 1914. She rightly suggests that improved methods of diagnosis and a greater clinical interest in pulmonary cancers of late years may be responsible for this, and it is evident that statistics gathered from the post-mortem records of general hospitals, while they give useful information on the nature of intrathoracic tumours, may yield very doubtful and conflicting evidence about the incidence of the disease either in the general population, or even in the wards of the hospital itself. Dr. BONSER'S paper has strengthened the suspicion that the much discussed increase in lung cancers may be no more than apparent. In Leeds the occupational incidence reveals nothing of significance. The age and sex incidence is similar to that found in most other hospitals, the proportion of male cases to female being about $3\frac{1}{2}$: 1. But Dr. BONSER shows that in Leeds the proportion of male to female autopsies is roughly 3 : 2, and she is to be congratulated on being the first writer on this subject to publish, along with the incidence, figures showing what proportion of all deaths in the hospital go to post-mortem examination. It will be seen that this information greatly helps in assessing the true value of the figures, for it indicates that the disproportion between the sexes is not so great as at first appears.

[2] THE LANCET, 1927, ii., 111.

Dr. T. C. HUNT'S paper, which appears on p. 759 of our present issue, treats the subject of cancer of the lung more from the clinical point of view, but attention is paid to the previous histories of pulmonary affections and their bearing on the ætiology. Of the 26 cases reported by Dr. HUNT from St. Mary's Hospital, half gave a history of previous disease of the lung. Influenza, which has been cited as an important ætiological factor, was reported in not more than a quarter of his cases. A similar proportion—about 30 per cent.—was revealed in a recent report by B. R. KIRKLIN, R. PATERSON, and P. P. VINSON on 68 cases of pulmonary tumour from the Mayo Clinic, and these authors justly remark that this incidence is not unduly high in view of the recent pandemics. Indeed, with the prevalence of the condition or conditions which the laity loosely term "influenza," it is surprising that so few of the patients claimed to have suffered from it. Tuberculosis, from these reports, does not appear to be a very common associate of lung cancer. BONSER found record of old or active tuberculosis in 26 of her 172 cases, HUNT finds it in only 2 in his 26, and KIRKLIN in none of the 68 cases from the Mayo Clinic, so that respiratory infections do not seem to play a very important part in the ætiology. Dr. HUNT draws special attention to the frequency with which pain marks the onset of symptoms in cancer, in contrast to phthisis in which pain is a comparatively uncommon early symptom. This is undoubtedly one of the most valuable points in differential diagnosis, and attention to it may make the early recognition of pulmonary cancer more certain. Perhaps many of the difficulties in diagnosis will be dispersed when it becomes more widely recognised that these tumours are fairly common, and are always to be borne in mind when investigating a chest case. The idea that lung cancers are little known rarities, only to be encountered once or twice in a lifetime, unfortunately dies hard.

Annotations.

"Ne quid nimis."

THE BRITISH CONGRESS OF OBSTETRICS AND GYNÆCOLOGY.

Dr. Gibbon FitzGibbon will preside over the seventh British Congress of Obstetrics and Gynæcology which meets at Dublin on the 24th of this month. The proceedings open with a discussion on the Management of Cases of Pelvic Disproportion, at which the speakers will be Prof. Munro Kerr, Prof. Fletcher Shaw, Dr. James Young, Dr. J. D. Barris, Dr. Bethel Solomons, and Dr. W. Taylor. This discussion will occupy both morning and afternoon, and in the evening the President and Mrs. FitzGibbon will entertain members of the Congress and their friends at the Royal College of Surgeons, St. Stephen's Green. Communications on the two following days are to include papers on metropathia hæmorrhagica (Dr. Wilfred Shaw), the complications of ovarian tumours (Prof. James Hendry), the use of glycerine in obstetrics and gynæcology (Dr. Caroline Elliott), double monsters (Dr. A. L. Mudaliar), eclampsia and its renal lesions (Mr. R. H. Paramore), mercurochrome in urinary infections in pregnancy (Prof. D. C. Rayner), the basic cause of cervical cancer (Dr. K. V. Bailey), fœtal death following quinine induction (Mr. A. A. Gemmell), the technique of radium application in uterine carcinoma (Mr. Gilbert Strachan), and pregnancy following X ray stimulation of the ovaries (Prof. Miles Phillips). The official guests of the Congress are Prof. John Osborn Polak, of New York, who will

contribute a paper on Follow-up Results in 500 Cases of Uterine Hæmorrhage of Non-malignant Origin, and Prof. Ludwig Adler, of Vienna. An exhibition of pathological specimens has been arranged in the Royal College of Physicians, and will be open for inspection after midday on Wednesday. Those who have specimens to show are requested to communicate with Dr. J. Lait, School of Pathology, Trinity College, Dublin, without delay; drawings or photographs of interesting cases or specimens being also welcome. The Congress dinner will be held at the Royal College of Surgeons at 7.45 P.M. on Thursday, the 25th, and the sessions will end at 1 P.M. on Friday, the afternoon being reserved for operative demonstrations. The hon. secretaries of the Congress are Dr. Bethel Solomons, Master of the Rotunda Hospital, and Dr. Gerald Tierney, 22, Lower Baggot-street, Dublin. The meetings will take place in the hall of the Royal College of Physicians in Kildare-street.

THE FLEA AT SEA.

ONE of the most important measures for preventing the spread of bubonic plague is the elimination of flea-bearing rats from ships. For some years now the English and Australian health authorities have been searching incoming ships for signs of rat infestation as a preliminary and guide to anti-plague measures. In 1925 C. V. Akin and G. C. Sherrard showed that rat infestation could be estimated very accurately, but when a ship is heavily infested no amount of fumigation seems to clear it. Several observers have shown that rats can be trapped on ships after fumigation, and this fact must be due to the presence of retreats in the ship's structure where rats can go but fumes cannot reach. For this reason rat-proofing of vessels has been advocated, for even if it does not in fact make the ship rat-proof it makes it much more vulnerable to fumigation. That it takes a long time to establish a rat-colony on a properly cleared ship has been shown in a recent paper by C. L. Williams, of the United States Public Health Service.[1] He investigated 1913 "ships" in New York harbour during two years, each fumigation counting as a "ship" in this enumeration. The rats were almost exclusively the black rat and his close relative the Alexandrine rat. As would be expected, twice as many rats were found on ships carrying a cargo suitable for rat food than on the others, and the nature of the cargo seemed to be the major rat-influencing factor. An outstanding result of the investigation was that the majority of rats are carried by relatively few ships and that most ships carry few rats. Only about 10 per cent. of the ships arriving at New York were heavily infested (more than 30 rats), and these are the vessels that constitute a menace to the public health. The really large rat colonies were found in ships fumigated at intervals greater than four months. Apparently the majority of ships return to their normal rat population about five months after fumigation, and ships found free of rats at one fumigation are usually free at the next one, whether this be two, three, or six months later. The obvious conclusion is that most ship rats are born on the ships they infest and that fumigation of every ship is a waste of money. Better results would be obtained by concentration on the few ships known to be infested. It is clear, however, that if this were to become the practice quarantine officers would have to keep a very careful look-out for new infestations, which do, of course, occur from time to time. For instance, a South American coaster yielded only seven rats on the first 13 fumigations while the fourteenth produced 143; the officers testified that the rats all came aboard in a single cargo of potatoes.

Another important observation made by Mr. Williams is that only two varieties of flea were found on ship rats in sufficient numbers to be of practical importance. These were *Xenopsylla cheopis* and *Ceratophyllus fasciatus*; other varieties were apparently only accidental passengers. His results agree with those of J. C. Gauthier and A. Raybaud at Marseilles, of W. Fromme at Hamburg, and of Newstead and Evans in Liverpool in finding *X. cheopis* by far the commonest flea. C. Tirboschi, at Genoa, S. Kitasato in Yokohama, and Schastry in Odessa found no other flea at all in their surveys of ship rats. The flea catch in New York varied quite definitely with the temperature, but humidity made little difference. Below 50° or 55° F. the numbers were very low, but the slower reaction rate of a fumigant in cold weather must be taken into account before assuming that there are far fewer fleas on rats in the winter. Probably both factors operate. Most of the fleas came from the Caribbean and the east coast of South America; ships plying only between northern ports harboured mainly *C. fasciatus* and did not seem to be a grave plague menace. The southern ships mostly carried rat-food cargoes, touched at many ports, and entered dock in most places. Sugar ships as a class had few rats and no fleas. The fumigant used had considerable influence on the number of fleas found; when Zyklon B was employed less than half as many fleas per rat were found as when generated gas or sprayed liquid were used.

As a result of his investigation Mr. Williams recommends that removal or closure of rat harbourages in ships should be required; that complete rat eradication should be substituted for the specified two hours' exposure to fumigation, and that ships should be fumigated on the basis of observed rat infestation, after giving due consideration to the potentialities for plague infection in each case. He adds that it is essential that inspections should be made only by highly efficient, conscientious, skilful employees who have undergone a lengthy period of special training.

[1] Public Health Reports, March 1st, 1929.

OLEOTHORAX.

INTRAPLEURAL injections of antiseptic oil were advocated by Bernou in 1922 in the treatment of purulent tuberculous effusions and pleuro-pulmonary perforations. For this purpose a volatile antiseptic dissolved in olive oil or paraffin was injected in an amount sufficient to fill the affected pleural cavity. The particular antiseptic used by Bernou was the somewhat mysterious French proprietary remedy known as gomenol, believed to be a distillate from the leaves of niavul (*Melaleuca viridiflora*). The success attained by the method soon led to its wider application, particularly in the treatment of progressive pleural adhesions in cases of artificial pneumothorax. A. Courcoux and A. Bidermann,[1] in a recent contribution, point out that the beneficial effects of oleothorax depend on its mechanical action in maintaining a positive pleural pressure and in separating pleural surfaces which would otherwise adhere and on its antiseptic action in chronic purulent tuberculous pleurisies. The success of artificial pneumothorax treatment is often threatened by the formation of pleural adhesions which cause a progressive reduction of the pleural cavity and a corresponding re-expansion of the underlying lung. In such cases the usual practice is to raise the pleural pressure and shorten the intervals at which refills are given, but the resulting benefit is, as a rule, only temporary. The substitution of oil for air prevents contact between pleural surfaces and enables a more constant pressure to be maintained. If success is to be obtained the pleura must be completely filled with the oil and rigorous control by X ray observations is essential. Undue mobility of the mediastinum which yields before a positive pressure and prevents adequate collapse of the diseased lung is another occasional cause of failure in artificial pneumothorax treatment. The authors suggest that in such cases small injections of oil may provoke local reactions, the formation of mediastinal adhesions, and consequent fixation. They hold that there is no evidence that the oil has a solvent action on adhesions,

[1] Paris Médical, 1929, xix., 15.

but that the pleura tends to thicken under its action. This effect may indeed lead to disastrous results, for in the presence of dense adhesions a weak-walled pulmonary cavity may rupture if the pleural pressures are raised too high. In purulent tuberculous pleurisies oleothorax is the method of choice if air replacement has failed to prevent reaccumulation or if secondary infection has occurred. Other indications for the induction of oleothorax are small pleuro-pulmonary perforations, too rapid absorption of air in an otherwise successful artificial pneumothorax, and when for any reason frequent refills are undesirable. In this country F.G.Chandler[2] has suggested oleothorax in the treatment of bronchiectasis, a condition in which artificial pneumothorax treatment seldom causes a satisfactory collapse of the diseased lung. Before commencing oleothorax treatment a preliminary injection of oil should always be given. If the pleural membrane is unduly sensitive a sharp reaction may occur manifested by pyrexia and effusion. In such cases caution will be necessary. Pleural shock may endanger life in this as in other forms of treatment involving pleural puncture. Too hasty raising of pressures may result in pulmonary rupture, while if a broncho-pleural fistula is patent the injection of oil may cause acute distress. A wise selection of cases and a careful technique are essential if success is to be attained.

PROGNOSIS IN HAY FEVER.

INOCULATION against hay fever should preferably begin by March, but many a sufferer from this complaint had forgotten what is in store for him until reminded by the spell of fine weather which we have been having. The practitioner faced with a request for prophylaxis will find guidance in an article,[3] contributed by Dr. John Freeman to our series on Modern Technique in Treatment, but, needless to say, a certain number of people are unwilling to take a course of injections unless convinced that they will gain a more than passing benefit. This question of ultimate prognosis has lately been dealt with by Dr. F. M. Rackemann,[4] of Harvard University, and it may be of interest to summarise his conclusions. "Every patient," he says, "wants to know what are the chances that the treatment of his hay fever in any one year will lead to results which will be permanent, and if not permanent, whether the immediate procedures will modify other treatment in later years." The answer to these questions is attempted by a scrutiny of the results of treatment, mainly by pollen injections, of 410 persons suffering from hay fever caused by ragweed. Only those who began their treatment in or before the season of 1925 and who were followed up for at least two years, are included in the tables. The number freed from the attacks for two successive years or more is disappointingly small—namely, 26, or 6·3 per cent. A review of the causes of this smallness shows several important features. Rackemann believes that a cure cannot be assured by persistent annual repetition of treatment; indeed, patients who need such annual repetition are unlikely to be cured by the methods at present available. In the small cured group the extent of the cure amounts to freedom for an average period of four years only. Thus far, and no further, do the present data warrant any conclusion. Statistics give the impression that the therapeutic extracts vary slightly in different years, and Rackemann goes so far as to say that "relief of hay fever is not always and necessarily dependent upon the particular treatment." These results, as he says, are distinctly disappointing, but more encouragement can be derived from his other deductions that an "improved" patient has a good chance of ultimately joining the "cured" group, and that in patients requiring annual courses, fewer and fewer inoculations will be necessary. The paper concludes with observations that dermal and general constitutional sensitiveness often persists long after clinical improvement is reached. Cure of hay fever by inoculation is clinical rather than truly immunological, and it is suggested that the conjunctival and nasal mucous membranes may become locally less sensitive.

[2] Tubercle, 1927, viii., 563.
[3] THE LANCET, 1927, i., 940.
[4] Amer. Jour. Med. Sci., March, 1929, p. 333.

THE POTATO AS CULTURE MEDIUM.

FOR the most distinguished research in the field of tuberculosis during the year 1928 the award of the American Association for the Advancement of Science has gone to Dr. H. J. Corper and Dr. Nao U'yei, of Denver. For some time these workers have been looking for a culture medium for the tubercle bacillus which would rival guinea-pig inoculation test in making a diagnosis. Of existing media Calmette's potato-cylinder was found to be the most efficient for growth of the bacillus in high dilution; but this medium had the disadvantage that it was also a suitable pabulum for contaminating organisms. In order to get rid of the latter the Denver doctors treat the supposedly tuberculous material with an equal volume of either 6 per cent. sulphuric acid or 3 per cent. hydrochloric acid and mix thoroughly in a centrifuge. Further, the growth-promoting properties of the potato-cylinder were enhanced by the addition of small quantities of a dye—viz., crystal violet—the most favourable dilution of this was found to be 1 part in 75,000. Their latest observations[1] show that they have been engaged in further simplification of their method and in comparing its value in practical tests on sputum, urine, and animal tissues with Petroff's method and with guinea-pig inoculation. They attempted to substitute a medium with ground potato for the crystal violet potato-cylinder broth medium previously described. At first they were unsuccessful, for the grinding in some way spoiled the potato. But it was found that if the potatoes are autoclaved for 30 minutes at 15 lb. pressure before being ground a successful glycerol-crystal-violet-potato-agar medium may be prepared. Exact proportions are still the subject of investigation, but it already appears that the glycerol content must be about 2–2½ per cent. and that the concentration of the dye should be only about one-fifth of that used in the potato-cylinder medium. In actual successes, or positive findings, the new method has proved equal to guinea-pig inoculation and definitely superior to the sodium-hydroxide-gentian-violet-egg medium. Among the practical advantages over guinea-pig inoculation may be mentioned economy, possibility of repeated observations, and the availability of a culture when positive.

THE XANTHOPROTEIC REACTION IN RENAL DISEASE.

THE grave clinical phenomena of true uræmia cannot with certainty be attributed to any of the substances investigated in this connexion such as urea, the amino-acids, uric acid, or creatin. It is only a few years since Becher and others have taken into particular consideration in investigating uræmic poisoning a group of substances of the aromatic series, such as indican, which are derived from intestinal putrefaction. Such substances, which are highly toxic, by their passage through the liver undergo a process of oxidation which renders them less toxic and rapidly eliminated by the urine. In normal conditions they are found in the blood in very small quantities, while in renal insufficiency they accumulate in large amounts. Becher with a special technique has instituted a xanthoproteic reaction to estimate the amount of soluble aromatic substances present in the blood. F. Tonietti, of the Institute of Clinical Medicine at Rome[2] has made a series of observations on 68 cases estimating the xanthoproteic reaction by Becher's method, using Ambard's formula

[1] Journal of Lab. and Clinical Medicine, 1929, xiv., 393.
[2] Policlinico. Med. Sect., xxxvi., March 1st, 1929, p. 163.

for the urea index, and Jolles's test for indican in the blood by way of comparison. He found in numerous patients with acute glomerular nephritis the reaction was within normal limits, the same being true of the indican and nitrogen content. In a case of uræmia with convulsions occurring during the course of acute nephritis with a high nitrogen retention the xanthoproteic reaction was negative. This is an interesting fact to which Becher has also called attention—namely, that in the course of acute nephritis even when convulsive seizures manifest themselves the permeability of the kidney to the aromatic group remains good. Negative results were obtained in patients with renal tuberculosis, syphilitic nephrosis, and in nephrosis of pregnancy. In cases of diffuse chronic nephritis in various stages in which symptoms of uræmic intoxication were absent, the xanthoproteic reaction showed a tendency to rise above normal, but in instances of grave symptoms of true renal insufficiency with more or less marked signs of uræmia the reaction reached a high degree indicating the retention of aromatic substances in the blood. The highest values were found in cases of uræmic coma and in primary or secondary renal sclerosis with uræmic intoxication. It is worthy of note that consecutive examinations showed an accentuation of the xanthoproteic reaction parallel with an aggravation in the symptoms and, on the other hand, it descended to normal limits with the disappearance of these symptoms. In these cases there is an evident agreement between the retention of aromatic substances in the blood and the occurrence of that form of uræmic that goes under the name of true uræmia in contradistinction to the slow and progressive course of grave toxic nervous symptoms of depressive type. On the other hand, in uræmia with convulsions the permeability of the kidneys to aromatic substances remains good and if this phenomenon is, according to Becher, a proof of a real difference between these two forms of uræmia, it is easy to understand how the evidence of an accumulation of such aromatic substances in the blood may have an important diagnostic value inasmuch as it allows these two forms of uræmia to be differentiated by a chemical reaction of very simple technique. There seems to be a certain degree of agreement between indicanæmia and the xanthoproteic reaction. In none of the patients with acute nephritis was the titre above normal, and all those with true renal sclerosis with more or less severe symptoms of uræmic poisoning showed a high titre, but while in some cases of uræmic convulsions the indicanæmia reached a high figure, in others with an equally grave symptomatology the amount was much lower. Hence the xanthoproteic reaction seems to be in greater agreement with the clinical symptoms of uræmia than does the amount of indican in the blood. From these observations of Dr. Tonietti it would seem that the xanthoproteic reaction is normal in cases of renal disease without renal insufficiency, and that in renal sclerosis it shows retention of aromatic substances in the blood when symptoms of absolute renal insufficiency make their appearance. Moreover, in true uræmia and anuria of whatever nature, the xanthoproteic reaction reaches high figures and this increase or persistence is of unfavourable import. Finally, although this reaction by no means always runs parallel with the level of indican and urea in the blood, it is in more constant agreement with the symptoms of renal insufficiency than the other two.

OCCUPATIONAL ANÆMIAS.

MUCH of our knowledge of the anæmias has come from occupational toxicology—from such apparently diverse sources as research on chronic benzene poisoning, toxæmias from amido- and nitro-derivatives of benzene, and the distribution of lead in the tissues in cases of plumbism. Facts associated with a fresh hazard now seem to link up the whole. This hazard is associated with the absorption of mesothorium into the body while applying luminous paints to watch-dials. Girls doing this work adopted the habit of pointing their paint brushes between their lips and so could in a week swallow from 7 to 200 microgrammes of radio-active substances, since the paint contained mesothorium and zinc sulphide. Not less than 15 girls who were thus employed in New Jersey broke down in health and died, often exhibiting symptoms similar to phosphorus necrosis, and a good deal of publicity in the United States has been given to these cases, much research being devoted to their elucidation. Dr. H. S. Martland, who has now summarised the whole story in two useful papers,[1] says that mesothorium when swallowed is absorbed and finally deposited, like lead, as an insoluble sulphate in the bones. Here it decays and disintegrates, giving off injurious alpha rays in the process. Should there be any septic infection, as, for instance, in the mouth, bone necrosis follows; but otherwise these injurious rays bombard and damage the neighbouring hæmopoietic bone-marrow. Hence may result leucopenic anæmia of the regenerative type with the presence of basophilic red cells, the condition, although more acute, recalling the anæmia of lead poisoning. Should this stage be survived, a more chronic type of disease may develop with low-grade crippling osteitis and aplastic anæmia. The condition of the blood now resembles that seen in chronic benzene poisoning, and apparently the marrow is so damaged as no longer to function. Contact with radio-active substances and X rays is a recognised cause of anæmia, either regenerative or aplastic in type. In the case of the New Jersey painters the existence of mesothorium was demonstrated during life by detecting emanations in their expired breath and after death by examining the tissues, when the bones in particular and the spleen were found to be depositories of this substance. No treatment can be of avail once the insoluble sulphate of mesothorium is laid down in the bones, and only time can help. Mesothorium decays half away in 6·7 years; in 12 years, therefore, a survivor should be safe. No case of poisoning has come to light in the watch industry in Europe or elsewhere, but only in America was the habit adopted of pointing the brushes with the lips. Knowledge of causation is naturally followed by abolition of risk, and so this occupational disease must disappear. But it will continue to live for the light it has shed upon the occurrence of anæmias.

THE METABOLISM OF THE ESKIMO.

THOSE conscientiously engaged in the elucidation of physiological problems by means of animal experiments must have constantly before their minds the knowledge that the results obtained with one species of animal may not necessarily apply to another species. Even different races or breeds of the same species of animal may show striking differences in their physiological behaviour. For instance, it has been shown that alone, among the breeds of dog, the Dalmatian has the capacity of excreting large amounts of uric acid in the urine. It should not, therefore, be altogether surprising if among the races of mankind we meet with fundamental differences in normal metabolic processes. The Eskimos are peculiar among human races in that their usual food consists almost entirely of protein and fat. Virtually the only source of carbohydrate in their diet is the glycogen present in the meat they consume, for the geographical conditions under which they live are such that, at least during the greater part of the year, it is impossible for them to obtain carbohydrate from any plant source. According to Heinbecker,[2] who has recently published a report on certain aspects of the metabolism of the Eskimos, from one-third to one-half of the total quantity of food eaten by them in cold weather is in the form of fat; in the warmer weather fat might furnish only one-seventh

[1] Jour. Amer. Med. Assoc., Feb. 9th and 16th.
[2] Heinbecker, P.: Studies on the Metabolism of Eskimos. Jour. Biol. Chem., 1928, lxxx., 461.

of the total quantity. Even when the maximal amount of fat is eaten, however, the Eskimos showed no signs of ketosis. The protein which makes up the rest of their dietary furnishes potential supplies of carbohydrate, and it has been suggested that such carbohydrate may be formed in sufficiently large amounts to counteract the ketogenic effect of the fat consumed. However, Heinbecker made some observations on the effect of starvation on the excretion of ketone bodies by Eskimos and found that they showed a very much milder degree of ketosis than is observed with fasting men belonging to other races. He suggests that there may be two fundamentally different mechanisms for dealing with fat in the human body, only one of which may require the simultaneous katabolism of carbohydrate. The Eskimos appear to need less carbohydrate to burn up fat than other races, and this may mean that their consistently low carbohydrate diet is associated with an increase in the effectiveness of that secondary mechanism which is independent of carbohydrate. He does not discuss the question whether this second mechanism is inherited in a peculiarly effective degree as a racial characteristic, or whether it is a result of individual adaptation to the prevailing dietetic conditions. The Eskimos were found to have an extremely good tolerance for carbohydrates. In fact, their blood showed rather less than the normal rise in sugar content after the ingestion of large quantities of sugar, and sugar never appeared in the urine under these conditions unless the subjects had previously been starved. There was, therefore, no hereditary or acquired alteration in their capacity for dealing with carbohydrates. One other point of interest emerged from Heinbecker's observations—namely, that the long-continued consumption of what would ordinarily be considered excessive quantities of protein had no demonstrable ill-effects on the Eskimos. They could deal perfectly well with the large quantities of nitrogenous material supplied to them and in no single case were signs of renal insufficiency met with. There is no need to assume that we are dealing here with any racial characteristic, for arctic explorers of European extraction have reported that after many years of living under similar dietetic conditions there have been no signs of any impairment in the efficiency of their renal or vascular systems.

RESEARCH ON ANÆSTHESIA: THE HICKMAN MEMORIAL.

THE appeal published in our correspondence columns, over the signature of Mr. Cecil Hughes, for initiating further research on anæsthesia is one that will commend itself at once to the medical profession in this country. It is noticeable that while the first great steps in anæsthesia, after its introduction in America, were British, yet of recent years new drugs, new methods, and new knowledge in connexion with anæsthetics are rarely our native product. The history of anæsthesia is one on which every Englishman, as well as every Scotsman, can look back with pride. The names of Hickman, Simpson, and Snow are inscribed for all time on the list of pioneers in this beneficent branch of practical medicine. Naturally we cannot expect a constant stream of great or original investigators in this work more than in any other department of scientific work. It looks, however, as though for some reason or another research work at all is altogether lacking or extremely scanty in Great Britain. Intratracheal administration of anæsthetics comes from America and spinal anæsthesia from the Continent, and although it is true that probably in the use of these methods and certainly in the use of general anæsthesia our practice is on a higher general level than that of Continental countries or even of the United States, yet it is to them rather than to ourselves that belongs the credit of initiating the methods which we pursue. The reason for this anomaly is not obvious. It may be that the practical Briton has been more concerned to perfect the human applications of anæsthesia as it is presented to him than to seek alternative and superior modes in the laboratory, or it may be that this particular and very difficult line of inquiry has not appealed to research workers because of certain inherent fallacies in the application of experimental results in anæsthesia to the human subject. Whatever the reason it is a pity that experimental research in anæsthesia should fall behind clinical excellence in this country. In some respects anæsthesia even at its best is still crude. Who, for example, can guarantee freedom from after-sickness in a formidable proportion of cases? Who, indeed, can tell the true pathology of this condition or supply anything but empirical remedies? Certainly improved technique has made this trouble less formidable than it used to be, but it is still one to be reckoned with, and supplies—even if there were no others—a first-rate problem for solution by research work in anæsthetics. We trust that the response to the appeal may prove sufficient to found a Hickman medal for original work.

THE OPHTHALMOLOGICAL SOCIETY'S CONGRESS.

DURING the last three days of this week the annual Congress of the Ophthalmological Society of the United Kingdom is being held in London, and there is every indication of a successful gathering. The subjects of the two principal discussions, on Thursday and Friday respectively, are Heterophoria and the Diagnosis and Treatment of Ocular Tuberculosis, the openers of the first being Mr. E. E. Maddox, Mr. Charles Goulden, and Group-Captain E. C. Clements, and of the second Sir Arnold Lawson, Dr. R. A. Young, and Mr. S. H. Browning. The morning of each day is being devoted to communications by individual members of the Congress, whilst for Friday afternoon, from 2.30 to 5, a clinical meeting has been arranged at the new Royal Westminster Ophthalmic Hospital in Broad-street, Holborn. By courtesy of Sir Joseph Petavel, F.R.S., the director, a visit is to be paid on Saturday afternoon to the National Physical Laboratory at Teddington.

Dr. T. Izod Bennett has been appointed Dean of the Middlesex Hospital Medical School in succession to Mr. Eric Pearce Gould.

Mrs. Margaret McGregor, of Stirling, has left £20,000 to the University of Glasgow to establish a chair in connexion with medical research.

PRINCESS MARY AT BRADFORD.—On Thursday in last week Princess Mary opened two infants' wards, a sunlight department, and a nurses' home at the Bradford Children's Hospital.

ANCOATS HOSPITAL, MANCHESTER.—The report of the medical board of this institution for 1928–29, submitted by the chairman, Mr. Arnold Renshaw, contains a summary of the extension of the methods of investigation to which many special types of disease are to-day submitted, and Mr. Renshaw indicated that during the next decade the special departments of Ancoats will require increased equipment to keep pace with modern knowledge and technique, laboratory work in particular having considerably increased in extent and application. In view of the extension of the municipal health services, and of the municipalities taking over the present poor-law hospitals, a greater onus, he points out, will be placed upon the voluntary hospitals to devote themselves to more specialised and serious disease, if by the force of an individual enthusiasm and zest for advancement and research they are to lead the van of medical progress. "The problem of the future," runs the report, "is how to apply these highly developed, precise scientific methods of individual diagnosis and treatment to patients in the mass without losing the thread of continuity of observation in any one patient." The solution of the problem is found to lie in finance, ample equipment and space, careful organisation, expert supervision, and enthusiasm.

The Clinical Interpretation of Aids to Diagnosis.

A Series of Special Articles contributed by Invitation.

XXVII.

THE SIGNIFICANCE OF ORGANISMS IN THE URINE.

I.—Preliminary Tests for Infection.*

The presence of organisms in the urine is direct evidence of an infection of some part of the urinary tract, provided that the specimen has been taken with due precautions against contamination from external sources including the urethral meatus and the surrounding parts. A cellular reaction almost invariably accompanies bacterial infection. No bacteriological examination of urine is therefore complete unless the cellular content is also investigated. Where possible, both cellular and bacterial content should be estimated quantitatively, otherwise no proper judgment can be given as to the significance of small numbers of cells or organisms. Furthermore, the analysis of the various types of cells present, and a search for casts and crystals, often furnish valuable help in locating the exact site of an infection.

Organisms and Cells in Small Numbers.

The presence in small numbers either of organisms or of cells does not necessarily indicate a pathological state. Quite commonly, a few meatal organisms, usually *Staphylococcus albus* or diphtheroid bacilli, find their way into a specimen during the passage of a catheter and yield a growth on culture; again, first morning catheter specimens from apparently normal individuals frequently contain a few leucocytes. The clinical history together with experience in the quantitative evaluation of such findings will usually decide whether they signify infection or pyuria.

Apart from meatal contamination, a point frequently raised is whether the finding of one or two definitely pathogenic bacteria in a catheter specimen of urine may not be due to a power possessed by the kidney of removing organisms from the blood stream—a question most often asked in regard to tubercle bacilli. It is now generally believed that a healthy kidney will not pass micro-organisms; that the presence of tubercle bacilli in the urine (excluding tuberculosis of the urinary tract below the kidney) implies a tuberculous lesion of the kidney; that in typhoid fever, septicæmia, or scarlet fever, whenever the causative organism is found in the urine, there must be a renal lesion which allows the organism to pass the kidney even though the lesion may be too small to produce renal symptoms.

Infection in the urinary tract may involve the kidney substance, the renal pelvis, the ureter, the bladder, or the urethra and its ducts. A positive bacteriological examination should assist in pinning down the infection to one or more of these sites if the organisms having a predilection for the various sites are known and if the bacteriological and clinical findings are correlated. From the practitioner the bacteriologist will require a properly collected specimen and a reasonable history of the case. The history, so often withheld, is of great importance in that it enables the bacteriologist to select the most suitable medium for obtaining successful cultures.

Collection of the Specimen.

A catheter specimen affords the only reliable positive information as to bacterial content, except when the urine is to serve simply as an index of urethral infection. Admittedly, it is not always desirable to use a catheter in practice, and it is a reasonable argument that if an ordinary specimen contains no organisms then a catheter specimen certainly will not. The preliminary examination of a "cleaned up mid-stream" specimen is therefore a useful procedure and, if negative, is entirely reliable; but if such a specimen contains organisms, catheterisation must be performed unless the bacteria can, with certainty, be classed as contaminants.

Catheter specimens should be received into a sterile flask or glass-stoppered bottle and should be examined as soon as possible after collection. If there is undue delay delicate organisms such as streptococci tend to die out, pus is liable to disintegrate and disappear, whilst, in hot weather, coliform organisms may so multiply that the number present gives a false idea of the severity of the infection. In all cases the first morning specimen supplies most information, and it is the only specimen of any value for quantitative and comparative work.

Males.—Non-catheter specimens from the male must of necessity contain the washings from the urethra; even a mid-stream specimen will contain prostatic or urethral pus and bacteria if infection in these sites is heavy. "Cleaned-up mid-stream" specimens are, however, relatively satisfactory as an index of infection of the bladder and higher parts of the urinary tract. When collecting a mid-stream specimen the urethral meatus should be washed, the first 20 c.cm. of urine passed into any vessel, and the remainder of the bladder contents passed straight into a sterile container.

Catheters are essential for obtaining representative bladder specimens if there has been antecedent gonorrhœa or prostatitis, and it is advisable to use a catheter in all males over the age of 50, owing to the frequency of mild chronic *B. coli* infections of the prostate. When examining for tubercle bacilli the specimen should always be taken with a catheter.

Females.—The cleaning up for bacteriological purposes of the external genitals of the female is difficult, and it is still more difficult to ensure that the urine is not contaminated with the numerous and varied vaginal and vestibular bacteria. Pus, epithelium, blood and mucus, all derived from the genital passage, are frequently present in the urine, and very few ordinary specimens of female urine are sterile on cultivation. Practically no reliance can be placed on the presence of pus and bacteria as indicating infection of the female urinary tract unless the specimen has been obtained with a catheter.

Children and Infants.—It is possible to catheterise even the smallest infant, but the procedure is not desirable when it can be avoided. Examination of a cleaned up specimen should always precede the passing of a catheter. Infants frequently pass water soon after they begin to feed. With patience a reasonable specimen of urine, uncontaminated with fæces, can be caught in a clean chamber if the infant is supported on the vessel held between the knees of the mother or nurse.

Ureteric Specimens.—When bacterial infection has been definitely located to the kidney it is frequently necessary to determine whether one or both kidneys are involved. This is particularly so in the case of tuberculosis. Ureteric specimens are best obtained with ureteric catheters passed by direct vision through a cystoscope—an operation requiring considerable practice and skill if injury to the ureter is to be avoided.

The Results of Preliminary Examination.

Examination of the urine for evidence of pyelitis is well worth while in all cases of fever of unknown origin, particularly in children, and in all cases of abdominal pain in which the diagnosis is at all obscure. The practitioner himself can rarely afford the time to do more than simple chemical tests for pus and blood, and examinations of the centrifugalised deposit or the deposit on standing.

The presence of pus in the urine can only be established with certainty by microscopical examina-

* The significance of the type of organism present will be discussed next week.

tion. Other methods, such as the caustic potash test or the ozonic ether test, only give positive results when much pus is present and they are in no way specific. Similarly, the guaiacum test for blood is extremely insensitive when compared with detection by the microscope. A simple microscope with a 1/4 in. and 1/6 in. objective is all that is needed in the majority of cases for obtaining evidence of bacterial infection, though a determination of the nature of the infection usually requires more elaborate apparatus and a more lengthy procedure.

Macroscopic Appearances.—Urine containing a large quantity of pus and bacteria has, when first passed, a characteristic sheen, whilst the turbid part rapidly settles to the bottom of the container in contrast to the slower deposition of amorphous phosphatic or uratic material. Though such an appearance is fairly characteristic the nature of the deposit should always be confirmed with the microscope.

Pus with Gonococci.—The macroscopic appearance of the urine is often used as a rough test of the state of the urethra and prostate in male gonococcal infections. For this purpose the urine is passed into two glasses, the first glass being an index of the condition of the anterior urethra, and the second glass that of the prostatic urethra. Obvious pus in the first suggests anterior urethritis, whilst "threads" or "commas" indicate that the prostate is involved. The procedure is sometimes elaborated by massaging the prostate before the urine is passed, so that the specimen contains prostatic secretion which can be concentrated with the centrifuge and examined for gonococci. This method yields less information than can be obtained from a stained smear of the prostatic secretion itself. It should always be borne in mind that pyuria in the male is not synonymous with gonococcal urethritis and that the continued presence of pus in the urine of a gonococcal patient merits investigation of the upper parts of the urinary tract.

Microscopic Appearances.

A drop of the urinary deposit is placed on a slide, covered with a slip and examined with the 1/4 in. and 1/6 in. objectives. A knowledge of sizes is of invaluable assistance in differentiating pus cells, epithelial cells, and red cells one from another or from foreign material such as droplets of oil derived from a catheter. Crystals and casts require more experience, but the commoner crystals, such as calcium oxalate or uric acid, and the general form of a cast can quite easily be recognised. Practitioners rarely find it an economical procedure to maintain a stock of bacteriological stains or a 1/12 in. oil immersion objective. When stained preparations are made, Gram's method with a suitable counterstain is the only reliable technique. Simple methylene-blue stained smears are useful as a guide, but in definite *B. coli* infections the bacilli can be seen with the 1/6 in. objective in an unstained preparation.

The practitioner, with his own microscope, can frequently find some evidence of urinary infection, though the exact nature of the infection usually requires a more elaborate investigation by a laboratory. Periodical examinations by the practitioner serve as a check on the progress of the more acute and definite infections, but it should be realised that any test, other than a cultural one, is almost valueless for estimating a cure.

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SALISBURY INFIRMARY LEAGUE.—The income of this league last year exceeded £11,000, and two beds have been endowed at the infirmary. The desirability of establishing a similar league for the middle class is being considered by the council in consultation with a number of public bodies in Salisbury.

Special Articles.

THE EVOLUTION OF HOSPITAL SCHOOLS:

COMBINED TREATMENT AND EDUCATION FOR CHILDREN SUFFERING FROM PHYSICAL DEFECTS.*

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THIS paper is designed to call attention to a movement which has almost imperceptibly gathered force and momentum during the last 20 years, is still increasing rapidly, is changing and is still further destined to change the whole outlook and future of the physically defective child of the elementary school type. While familiar to some social workers, educationists, and others especially interested, its importance is as yet hardly appreciated or understood by the general public. It is especially desirable that it should be recognised by and secure the support and sympathy of the medical profession, as it is a matter which is primarily dependant on expert medical help and guidance.

While much of what follows refers to the crippled child, we would urge that the term physically defective in this connexion should not be confined to the cripple, but rather be extended to embrace all those children, other than the mentally defective, who show pathological deviations from the normal of such a degree as to make desirable special provision for combined medical and educational treatment, whether temporary or prolonged.

And here let us emphasise that the first and essential responsibility for the management of such children rests, not with the teacher but with the doctor. Children may be divided into two broad groups: those who are well and those who are not. For the latter, every endeavour should be made to achieve restoration to normal health whether the disability be of short duration or chronic in type. One would imagine such a statement to be self-evident. In acute illness it is accepted, but in chronic disability it is not. It is our purpose to direct attention to this matter, and we feel that prolonged experience in the management of the disabled child is not only a justification for a plea on his behalf, but also a responsibility which makes such a plea necessary.

The Chronically Disabled Child.

For the chronically disabled child of the working-class parent we shall proceed to show that almost nothing was done in the way of combined treatment and education until the present century; but during the last 30 years the outlook for such children has undergone revolutionary and beneficent changes. For other children, there is little advance to be recorded. For the secondary or public school child, on the other hand, there is no State aid, no guiding organisations, almost no specially staffed and organised institutions—no corporate life with its wider outlook, its spur to ambition, its competition, its scope for achievement and advance, its morale and discipline, its inviting threshold to active and useful adult life, with all its opportunities and responsibilities. The greatest bar to their progress is the inability through lack of knowledge of their parents to realise their children's potentialities and how they may best be catered for, and the lack of opportunity of obtaining

* A paper read before the Medical Officers of Schools Association on March 15th.

the necessary help. The more severe cases are usually tenderly cared for in their own homes, shielded from those stimulating influences which should so improve their character and moral fibre, and denied the opportunity of exercising those gifts of aptitude and intelligence with which, as a rule, they are richly endowed. The less severe cases attend day schools perfunctorily or are drafted to so-called schools for delicate children. A few struggle through ordinary schools, but handicapped by afflictions which might often be remedied, do not get their full chance and, their sensitive natures exposed unhappily too often to the derision and scorn of their schoolmates, stand grave risk of being warped and soured. A schoolboy or girl may often unthinkingly be a little beast to his afflicted fellow. How many of us realise the sufferings of the unhappy victim of nocturnal enuresis in the ordinary school? And that is a comparatively trifling example. This is deplorable, as the potentialities of these afflicted children are immense, both to the community and to the individual. Their very defects may not infrequently in skilled hands be turned to advantage. A very real effort should be made on their behalf.

Historical Survey.

One of the most profound changes which has taken place in English elementary education during the last 20 years has been the direct attention given to the physical condition of the child. It has gradually been realised by school authorities that each child must be dealt with as a growing individual whose mental capacity and development is dependent on his health and physical fitness. Taking first and chiefly the cripped child, throughout history his has been an unhappy lot. The Spartans with eugenic motives took their cripples to the hill tops and killed them.[1] The Athenians allowed theirs to die from cold and neglect.[2] Similar treatment has been common amongst many savage races with less justification. In mediaeval times in our own country the cripple was coupled in men's minds with malignity. It was assumed that the crippled in body were crippled in mind too; and they must often have become so as a result of the attitude of others to them. As Sir Robert Jones has said:

"Just as the mediæval witch became obsessed by the enshrined belief in her own devilment, so the cripple, taunted, shunned and persecuted, found refuge in a mind as distorted as his body. This perversion of character, as familiar in Shakespeare's 'Richard III.,' as in Dicken's 'Quilp,' or Hugo's 'Hunchback of Notre Dame,' presents the bitter revolt of men in exile and contempt."

Where such ideas did not predominate, the attitude was one of ridicule. The hunchback was chosen to be the jester of the court. With the Reformation crippling deformity was considered emblematic of heavenly wrath, and the cripple was cast more completely than ever from the pale of society. Nevertheless, in innumerable instances throughout history cripples, in spite of their physcial disabilities, have achieved distinction and exercised important influence.

The first legislative provision for cripples which we can trace was in 1601 when custody only for cripples was allowed by the Poor Relief Act. When attention was being drawn generally to child welfare during the industrial revolution of the nineteenth century interest became rather more concentrated on the cripple. But he was then regarded as a mere object of pity. Charles Dickens aroused interest by depicting very truly the attitude of the public in his day to the cripple and the attitude of the cripple, perforce, to himself, with no thought or hope of cure, but a more or less cheery philosophy and acceptance of his inevitable fate. It was generally understood that if they survived, their deformities were likely to render them useless as citizens. Cases congregated in homes for incurables and workhouse infirmaries, or were hidden in the recesses of their own homes with no books, toys, or interests. Here and there a philanthropic worker would make some effort to give them help and add to the interest of their lives. An early pioneer was Lord Shaftesbury, who did so much to win the sympathy and help of the public for these unfortunate children.

In 1851 and 1865 two industrial homes were founded for older cripples which are still in existence. The one was the Cripples Home and Industrial School for Girls in Marylebone (now transferred to Winchmore Hill), and the other was the National Industrial Home for Cripple Boys at Kensington.

When the Education Act of 1870 made elementary education compulsory no cognisance was taken of children who by reason of mental or physical defect could not attend or profit by ordinary school. During the 10 years preceding the beginning of the twentieth century a few efforts were made by individuals to start little schools for some of these crippled children and the Board of Education, as an act of grace, allowed them to rank as infants schools for purposes of grant.[4]

The first real move for the cripple, however, was taken by Mrs. Humphrey Ward. She made use of the Passmore-Edwards Settlement off the Gray's Inn-road, which had existed as a play centre, and with the help of friends on the London School Board opened in 1899 a small school for 25 invalid and crippled children. This was the first day school for physically defective children to be supported out of public rates.

In 1893 the first step had been made in specific legislation for defective children by the Elementary Education (Blind and Deaf Children) Act enabling local education authorities to deal with children of this category in their area. Cripples were left out simply because it had never occurred to persons in authority that they merited consideration. Mrs. Humphrey Ward, with the support of the committee of the Passmore-Edwards Settlement and the newly gained interest of the London School Board, then urged the extension of this Act to include other defective children. The passing of the Elementary Education (Defective and Epileptic Children) Act of 1899 was a result of this, and for the first time gave statutory power to local authorities to deal with the education of the cripple child. Though permissive only, it gave them the power to make arrangements for ascertaining what children in their area were suffering from such physical defects as made them incapable of receiving proper benefit from instruction in the ordinary elementary school, and for providing for the education of such children. The first day school for cripples, to be certified under this Act, was this Passmore-Edwards Settlement School, which was certified in 1900. The first residential cripple school to receive official recognition was the Heritage School of Arts and Crafts, Chailey, Sussex, founded and conducted by Mrs. Kimmins. In 1905 the Manchester Education Committee established the first municipal residential school for physically defective children at Swinton House.

Such developments are of special interest when one recollects that it was not until 1907, by the Education (Administrative Provisions) Act, that the School Medical Service was inaugurated. This is the most important landmark in legislative attempts to improve the lot of the physically defective child. Under the wise, statesmanlike, and sympathetic guidance of Sir George Newman an entirely new era was opened for the defective child, and while much still remains to be done, almost incredible advances have been made with incalculable benefits both to the individual and the community.

No immediate measures followed this Act. For financial reasons local authorities were encouraged rather to coöperate with voluntary agencies than seek assistance from the Board of Education on behalf of the debilitated crippled children in their areas.[5] But all the time public sympathy was being further enlisted and public opinion educated to the needs of the debilitated and crippled child.

The Experiment at Alton.

In September, 1908, the Lord Mayor Treloar Hospital and College was opened in the derelict Princess Louise Military Hospital at Alton. Sir

William Treloar was a philanthropic but shrewd man of business. Inspired by Charles Dickens' "Christmas Carol" to help cripple children, he had inaugurated some years previously a crippled children's Christmas Hamper Fund. He soon realised what a small proportion of the physically defective children of the metropolis were receiving adequate medical attention. Country hospitals for such patients were unknown. No institution existed which combined expert medical aid, education, and technical training. Treatment in the few cripples' homes was either non-existent or so notoriously bad that the term cripples' home was associated with pity and contempt. Orthopædists had not even considered the wider and essential issues of combining with adequate treatment, education, and technical instruction. Philanthropists who were interested in cripples took for granted that surgical skill could do so little that provision for specialised treatment was hardly called for, and the cripples' home was a mere asylum for sheltering the unfortunate recipient of its charity.

The scheme originated by the late Sir William Treloar is still the most perfectly adapted to the full needs of the cripple child with which we are acquainted. Briefly, it comprises the treatment of the cripple by the most modern orthopædic methods with preference to conservative treatment in surgical tuberculosis, in an open-air country hospital situated in a specially suitable locality. In addition to specialised methods of local treatment the importance of rest, exercise, open-air, and sunlight has been recognised and utilised to the full from its inception. To these have been added artificial light treatment since 1912 and seabathing for therapeutic purposes since the establishment of its seaside branch at Hayling Island immediately after the late war. During treatment, and since the foundation of the hospital, children have received education, and this without grant from the education authorities for the first five years of its existence. From its inception there has been practised a carefully planned system of after-care designed on the broadest medical and social lines.

For the adolescent cripple, for whom further surgical aid could not be given, technical training combined with specialised education in a separate institution, but under the same management, has been employed from the outset. Boys admitted to this department of the hospital's activities—the College—receive training for three years in a trade suited to their limitations. On completing their training they are assisted to find permanent employment. By means of an old boys' association contact with them is maintained after discharge and they are helped and encouraged by every possible means and assisted to fresh employment if and when required.

After the passing of the Act of 1907 progress became more rapid. By the Finance Act of 1911 £1,500,000 was put aside for sanatorium work and the like, both children and adults benefiting.[6] In 1912 further grants were given. In the same year pulmonary tuberculosis became notifiable and this helped to diminish infection and trace more easily cases of surgical tuberculosis. Meanwhile 62 day and residential schools for the education only of cripple children had been established accommodating 4617 children and certified as "special schools" by the Board of Education. Fifty-five of these were receiving an annual grant from the Board.[7]

It had been realised already that prolonged treatment was advisable in special sanatoriums under constant expert medical supervision for children with acute tuberculous infections of the bones and joints and that stay in sanatoriums was advisable until complete arrest of the disease had been secured, a period often of 18 months to two years, or even longer. Yet not in one case in special school or in hospital had education and treatment coexisted officially. The Lord Mayor Treloar Hospital, however, at Alton, had, as already stated, on its own responsibility and from its inception in 1908, been offering educational facilities to its patients.

Under the Elementary Education (Defective and Epileptic Children) Act of 1899 the hospital was certified as a "special school" for 40 life-children in May, 1913, when two qualified teachers were appointed. These teachers took charge of the convalescent children who were taught in the school-room or the forest school. The Chief Medical Officer in his report to the Board of Education for 1912, having sketched the above, continued as follows:

> "The medical superintendent and the trustees, however, were desirous that the arrangements for teaching should be extended so as to provide for children who were still confined to bed. In view of the special circumstances, and in order to overcome the difficulty of introducing effective ward-teaching into an institution which is primarily a hospital and not a school, the Board agreed to sanction an experimental scheme. Under this scheme the school was to be certified for 150 children and the staff to consist of four fully qualified teachers."[8]

And the report concluded with a remark on the difficulty of grafting such an educational scheme on to existing hospital arrangements, as if it was very conscious it was venturing on untrodden ground, and emphasised the necessity of sympathetic coöperation and give and take between the nursing and teaching staffs. This, then, was the first "hospital school," the first recognised attempt to cure and educate the cripple at one and the same time.

Lord Melchett, then Sir Alfred Mond, Minister of Health, speaking at Alton in 1922, referred to this as follows:

> "Sir George Newman had just reminded him that when the Prime Minister visited the (Treloar) hospital in 1911 he was so struck by the important work being done there that he then and there decided to start the giving of grants to make it possible for the work done there to be extended throughout the country. The hospital was a great monument and was a milestone on the road leading to the increased care and welfare of children."[9]

Changing Outlook for the Cripple.

The importance of this official recognition and approval will be readily realised. Other hospitals soon followed and within a year Heswell, Woodlands (Birmingham), and Leasowe (Cheshire) were also approved by the Board for purposes of grant. Gradually but surely the outlook of the cripple, notably the tuberculous cripple, was changing. But with the general public, even among educated people, crippledom was still considered a condition which did not merit much attention, it not having been realised that the cripple could be of any appreciable economic value to the nation. Where the local authorities had attended to the education of the crippled child in their area this was in the vast majority of cases arranged for in schools for the mentally defective. This is so even now in some areas. The blind, the deaf, the epileptic, and the mentally deficient were earlier and better catered for than the cripple. Indeed, when in 1914 the Amended Elementary Education (Defective and Epileptic Children) Act was passed putting a duty on the local educational authority to make suitable provision for the education of mentally defective children over 7 years of age, no thought was taken of the cripple child for whom as yet no compulsory measure had been passed by Parliament.

Then came the war with its inevitable toll of crippling among the adult male population. In the words of Sir William de Courcy Wheeler:

> "The success which followed the stupendous effort of the medical profession and its allies to restore maimed and crippled soldiers to a normal condition of useful citizenship awakened Britain and America and most of the civilised world to the fact that crippledom amongst the civil population was an unnecessary and avoidable evil."[10]

At the same time "returns" from cripple schools were showing that 70 to 90 per cent. were being discharged fit to compete in the ordinary industrial life of the nation. The cripple, hitherto a menace to society, was being proved capable of taking his own stand in the world. In other words, his combined treatment and education were worth while. The

London Education Committee Return for Cripple Schools in 1917 states that:—

Concerning 1609 children leaving 36 certified day schools in the three years ending March 31st, 1918:—

Passed out below 14 as physically fit to attend ordinary public elementary schools	345
Exempt at 14 as being no longer physically defective ..	94
Exempt between 14 and 16 for suitable work	768
Left school at 16 because of age limit (of these 70 per cent. fit for suitable work)	366
Obtained scholarships in various technical and commercial schools	36
	1609

In 1918 the Amended Elementary Education (Defective and Epileptic Children) Act of 1914, already alluded to, was extended to include the physically defective. It required the local authority to ascertain what children in their area were physically defective or epileptic and to make provision for their education as per Section 20 of the Fisher Education Act. Actually this section of the Act did not come into operation until 1926 and even now is not strictly enforced.

Meanwhile, however, from various reports it soon appeared that ½ to 1 per cent. of children of school age were requiring treatment and education as cripples—i.e., 30,000 to 60,000.[12] Investigations into the causation of crippling defects in school-children brought out a number of interesting points. Diseases of bones and joints (mostly tuberculous), infantile and other forms of paralysis, congenital defects, rickets, and accidents were chiefly responsible. Rheumatism rarely produces joint disease and crippling amongst children, though amongst adults the toll is high. Tuberculosis headed the list as an individual cause in children, and in order of frequency spine, hip, knee, and ankle. Poliomyelitis followed closely.[13] It is noteworthy that the age of onset for all types of crippling falls predominately in the years preceding ordinary school life; for the majority of cases of tuberculosis arise between the ages of 1 and 6, and of poliomyelitis the same, while rickets is essentially a disease of the first year or so, and congenital defects must also be included. As these figures of the early onset of crippling deformities were brought to light and as many years of medical inspection showed that a proportion of 30 to 40 per cent. of children on entering school at the age of 5 require medical treatment for various causes,[14] largely a result of neglect, new regulations were passed under the Education Acts of 1920 empowering local authorities to provide educative treatment and therefore medical supervision from the age of 2 upwards.

The importance of the physical, social, and general welfare of children of pre-school age had long been realised. Nursery schools for such children had been inaugurated by voluntary enterprise some years previously, and by the Education Act of 1918 their establishment and promotion had been officially recognised and grants provided in their aid. This later work on the age of incidence and causation of physical disability gave fresh impetus to the movement on their behalf, and an earnest attempt was made to correlate for them the work of the various health, educational, and general welfare organisations. By 1926 there were 99 day nurseries for 3354 children and 26 residential nursery schools with accommodation for 1367, but the greater number of these were still dependent on voluntary committees.[15]

These schools by overcoming the effects of the too-frequently insanitary and mentally and physically unhealthy environment of the homes from which many of the children come; by encouraging the natural unrestricted development of the children's mental and physical resources, whilst instilling appreciation of the principles of healthy living, of fresh air, wholesome food, and regular hours; and by the additional benefit gained by the modicum of discipline and education given, have proved indisputably their very great value and their promise.

At the same time as this legislation was being extended to provide for the older child with physical debility, as already stated, technical training for the adolescent cripple had been commenced as early as 1851, and such training combined with treatment was started at the Treloar College in 1908. These efforts were recognised officially in 1911 but the legislation was now further extended, giving opportunity for comprehensive schemes for vocational training on various lines with substantial provision of grants.†

Incidence of disability as it occurs amongst elementary school-children is well shown by Dr. (now Sir William) Hamer's report on this in the London area in 1919 as follows:[16]

Pulmonary tuberculosis	1,614
Surgical tuberculosis	3,507
Other crippling defects	5,407
Heart crippling	2,291
Delicate or otherwise unsuitable for ordinary school ..	17,228

To the Chief Medical Officer of the Board of Education it appears that the child who is in a chronic state of subnormal health now constitutes one of the most serious problems of the School Medical Service.[17]

References.

1. Garrison, F. H.: Abt's History of Pediatrics. Philadelphia and London, 1923, p. 35.
2. Meissides: Janus, 1914, xix., 289.
3. Jones, Robert: The Cripple, Oct., 1928, p. 5.
4. Hill, A. H.: Ibid, p. 41.
5. Report of Chief Med. Off. Board of Education, 1911. Footnote to p. 117.
6. Ibid., par. 80.
7. Ibid., Section viii., par. 140.
8. Report of Chief Med. Off. Bd. of Educ., 1912, par. 80.
9. Hampshire Herald, July 7th, 1922.
10. Wheeler, W. de C.: Cripples Journal, Oct., 1924, p. 54.
11. Report of Chief Med. Off. Bd. of Educ., 1917, par. 111.
12. Report of Chief Med. Off. Bd. of Educ., 1919, par. 145.
13. Ibid., pars. 146, 147.
14. Health of the School Child, 1923, p. 82.
15. Health of the School Child, 1926, p. 38.
16. Report of Chief Med. Off., Bd. of Educ., 1919, par. 157.
17. Health of the School Child, 1926.

(To be concluded.)

SCOTLAND.

(FROM OUR OWN CORRESPONDENT.)

Aberdeen Joint Hospital Fund.

THE Aberdeen Joint Hospital Fund of £400,000 is now closed. This is not only a personal triumph for Lord Provost Lewis, but a great achievement for the north-eastern region of Scotland. It has taken only two years to raise this sum. In the last month Lord Provost Lewis called for £30,000—that is, £1000 a day—and he got it! He has done even better, for he took up a friendly bet of £5000 that he would not get his last £30,000 in a month. The bet has been handsomely paid and this £5000 has been added to the £400,000. With this and certain other subscriptions there is now some £7000 more than the total asked for.

The story of this fund is a romance of generosity. Lady Cowdray began it two years ago with £25,000; Viscount Cowdray gave another £25,000, and two similar gifts from Sir Thomas Jaffrey and Sir Robert Williams completed the first £100,000, but there have been shoals of small subscriptions and the whole north-east of Scotland was roused to a great effort. Of the total, it is expected that £107,000 will go to endowment.

The whole scheme is now safe, and Aberdeen now leads Scotland on two issues—by the coördination of its public medical services and by the splendid impulse given to the voluntary hospital movement.

Scarlet Fever Antitoxin.

Dr. C. Barclay Reekie, medical officer of health for Dunfermline and medical superintendent of West Fife Joint Hospital, records his experience in a considerable epidemic of scarlet fever, where the overcrowding of the hospital during the winter months had been

† For detailed report see Education Act, 1921, Part V., Grant Regulations, No. 19, and the 1925 extension to this Act, the so-called "Board of Education (Special Services) Regulations."

considerable. He states that they emerged without one fatal case, and attributes this largely to the use of scarlet fever antitoxin. "Its routine use," he is reported as saying, "had undoubtedly diminished the average length of stay of scarlet fever patients in hospital, and on many occasions during intensive overcrowding it was only its employment that made the admission of fresh cases at all possible. At first it had been thought that the expense of using antitoxin might not be justified, in view of the fact that scarlet fever did not endanger life to the same extent as did diphtheria; but experience had made it quite clear that they had an invaluable remedy, which, if used early in the disease, would prevent complications and greatly shorten the period of disability. The duration of residence now attained was the lowest on record, and there was no doubt that a saving had been effected in the cost of board of patients which more than covered the additional expense entailed. Furthermore, there had been a reduction in permanent disability resulting from complications of the disease." The experience in Scotland was summarised in the Board of Health annual report for 1927, and Dr. Reekie's clinical data are in line with observations elsewhere. But scarlet fever immunity is not a simple problem and it is too early to formulate definite conclusions. This experiment, however, in a small provincial hospital, is an indication of how rapidly the new ideas in public health are being applied practically. Over 30 years ago clinical experiment had begun with diphtheria antitoxin; but diphtheria is still with us in somewhat larger numbers than before, and the conquest of scarlet fever is not likely to be more rapid.

Influenza Vaccine: An Edinburgh Experiment.

This year Lieut.-Colonel W. Glen Liston, at the laboratory of the Royal College of Physicians of Edinburgh, has had the opportunity of testing the effects of influenza vaccines. The results, though important as far as they go, are not conclusive, and Colonel Liston does not regard them as more than the beginning of an investigation. In the recent epidemic 700 Edinburgh people were inoculated with a vaccine prepared almost on the lines of the vaccine recommended by the Government in 1918. The chief difference was that it contained more of the influenza bacillus than the 1918 vaccine. Its object was to vaccinate persons against both influenza and its complications. Colonel Liston had to depend on volunteers. In some cases whole staffs submitted to vaccination, but in other cases only a few. As the epidemic was in progress no time was allowed for the vaccine to produce immunity before exposure. As a preventive measure, therefore, the experiment had little chance of succeeding. But those vaccinated, and afterwards contracting influenza, seem to have suffered far less severely than the unvaccinated.

The results obtained in the case of the scavenging staff of Edinburgh Town Council, which are tabulated below, bear this out:—

	Vaccinated.	Not vaccinated.
Total of outdoor staff, 990 ..	139	851
Off work with influenza	13	78
Total number of days off	136	1096
Average days off per man	10·46	14·05
Percentage attacked	9·35	9·16

The important points to bear in mind are that in the case of the unvaccinated the period of sickness was longer, and that influenza attacked both classes in practically the same proportion.

The figures in this table are supported by figures obtained in connexion with a business house in the city. Of its staff 51 were vaccinated and 140 were not vaccinated. Out of the 140, 9 had influenza; out of the 51, 5. But while the attack lasted many days in the case of the former, it lasted but two days in the case of the latter.

Correspondence.

"Audi alteram partem."

PUBLIC HEALTH CONGRESS IN ZURICH.

To the Editor of THE LANCET.

SIR,—The preliminary programme for the 1929 Zurich Conference of the Royal Institute of Public Health, May 15th–May 20th, has now been issued and a copy can be forwarded on request. We are assured of the most cordial welcome by the Swiss National Government, the authorities of the Canton, City, and the University of Zurich, and by the leaders of the medical school of Zurich.

Invitations have also been received to visit various health stations in Switzerland. The Government gives a concession of 50 per cent. on the State Railway; free transportation will be provided on the Rhaetian Railway, Chur to Davos, and on the railways, Chur to Arosa, Sierre to Montana, and Aigle to Leysin. The local authorities at each of these well-known centres are most anxious to welcome as many members of the Congress as possible. We are further assured by the Czecho-Slovak Minister, Mr. Jan Masaryk, of a hospitable reception for those who may find time after the Congress to extend their journey to the two great Czecho-Slovak spas of Carlsbad and Marienbad.

In order to complete arrangements for the comfort of members of the Congress desiring to participate in the extensions it is essential that we should know immediately which of the visits members will desire to take. Particulars regarding the extensions and the routes to be traversed, together with information as to the expenses to members of the Congress, will be forwarded on application; non-members may accompany members, but will not be able to enjoy all the special privileges. The inclusive cost of the visit to the Congress at Zurich will range from £10 4*s.* 6*d.* for the short sea route, second-class travel on the Continent and hotel accommodation, to £12 12*s.* 6*d.* for first-class travel throughout and hotel accommodation.

Full particulars regarding the different extended journeys available after the Conference, together with a list of the various hotels in Zurich, is available on demand, and it is earnestly desired that all who propose to attend the Conference will communicate with us as soon as possible.

We are, Sir, yours faithfully,
E. W. HOPE, O.B.E., M.D., B.Sc.,
T. N. KELYNACK, M.D., M.R.C.P., J.P.,
Hon. Secretaries.

Royal Institute of Public Health,
37, Russell-square, London, W.C.,
April 3rd, 1929.

THE EMPLOYMENT OF BACTERIA IN MODERN WARFARE.

To the Editor of THE LANCET.

SIR,—Profs. Pfeiffer and Prausnitz are men of great scientific distinction who may be presumed to be competent to listen dispassionately to evidence, to examine it critically, and to give a true verdict. I ask them to bend their minds to this simple problem:—

In January, 1918, a laboratory attached to our 5th Army reported the isolation of bacteria, resembling bacilli of plague, from material dropped by a German balloon. This discovery is officially confirmed in our "History of the Great War." From this I quoted textually in my speech, and was therefore "sure of my facts."

No evidence to refute the official statement has ever been produced. There have been, it is true,

vehement though vacuous denials by interested persons acting perhaps under instruction; but there is not one shred of evidence which has ever impugned the accuracy of our laboratory investigation. I therefore assume that my eminent colleagues must conclude, however reluctantly, that this discovery of bacilli is not open to doubt. I next assume that the hypothesis of spontaneous generation of bacilli has been abandoned. I venture, therefore, to summarise: the bacilli were found; they did not arise spontaneously; they must have been introduced into the material in which they were discovered; no one had access to this material before it was dropped in our lines, but units of the German Army.

Accordingly, I invite Profs. Pfeiffer and Prausnitz to rid themselves of prejudice, and after considering this evidence to join with all dispassionate people in passing a verdict of Guilty against the German Army upon the odious charge of employing bacteria as instruments of war.

I am, Sir, yours faithfully,

Portland-place, W., April 5th, 1929. MOYNIHAN.

GALLOP RHYTHM.

To the Editor of THE LANCET.

SIR,—In the course of the interesting annotation on this subject that appeared in THE LANCET last week (p. 729) two types of gallop rhythm are said to have been described, whereof the one depends upon apparent reduplication of the first, and the other of the second cardiac sound. This is true, but the description perpetuates confusion.

In the *bruit de galop*, described by Potain, the first sound appears to be reduplicated and, whatever the explanation and significance, the rhythm is that of a galloping horse's hoof-beats: two sounds in rapid sequence, and a third after a definite interval. Only this sequence, which is that of a gallop, should be called galloping. What is wrongly spoken of as galloping rhythm, due to apparent reduplication of the second sound of the heart, is not a galloping rhythm at all, but that which C. J. B. Williams, 90 years ago, rightly called cantering rhythm, for the rhythm is that of a cantering horse's hoof-beats; one sound, an interval, and then two sounds in rapid succession. This sequence gives what the French rightly call the *bruit de rappel*. It recalls the heavy blow of a smith's hammer on the object being forged, followed by two shock-absorbing taps on the anvil.

Thus, apparent reduplication of the first sound is galloping rhythm, *bruit de galop* or (frequently) Potain's murmur. Apparent reduplication of the second sound may be called *bruit de rappel*, or cantering rhythm, but should never be called "gallop rhythm" for the best of all reasons—that it does not resemble the rhythm of a galloping horse's hoof-beats. The whole matter is admirably set out in a little book now insufficiently read—namely, Gee's Auscultation and Percussion.

I am, Sir, yours faithfully,

F. G. CROOKSHANK.

Wimpole-street, W., April 5th, 1929.

BLOOD STANDARDS.

To the Editor of THE LANCET.

SIR,—The inaccuracies in the ordinary blood count are well demonstrated by Dr. Dyke in your issue of March 30th (p. 681), and all pathologists will support him in requiring from instrument-makers a statement of what they mean by normal. The matter could well be carried further and a definite arbitrary normal agreed upon for all instruments.

The Haldane hæmoglobinometer is probably the most accurate in its method of comparing a sample with the standard scale, but unfortunately the latter is set far too high. In my experience the normal with this instrument ranges from about 78 to 85 per cent. and a reading of 100 per cent. is almost unknown. It is evident that a true reading can only be obtained by adding 20 per cent. to the Haldane figure. I believe this excessive standard to be chiefly responsible for the statement that the colour-index in pernicious anæmia is frequently below one and is of small value in diagnosis. The Tallqvist method is not as finely graduated as the Haldane, but I find that it gives a more reliable estimation because its standard is set nearer to what experience indicates to be the true normal.

The colour-index as at present rendered is of little value by itself. Thus an index of 1·1 in a red cell count of five millions indicates that the red cells are more or less normal, but the same index in count of two millions denotes serious derangement. I therefore suggest that the index be followed by the letter E (for erythrocytes) and a digit representing the nearest million of red cells in the count. In this way the first example would read 1·1(E5) and the second 1·1(E2), thereby giving a definite significance to the index.

I trust that the matter that Dr. Dyke has raised will not be allowed to drop, but that concerted action will be taken.

I am, Sir, yours faithfully,

C. E. JENKINS.

Pathological Department, Salford Royal Hospital, April 5th, 1929.

HICKMAN MEMORIAL FUND.

To the Editor of THE LANCET.

SIR,—A committee meeting of the Hickman Memorial Fund was held on March 27th, at which Lord Dawson presided. The possibility of fulfilling all the objectives of the appeal was fully discussed. It was decided that the Fund was, as yet, inadequate to restore Hickman's tombstone, to provide a memorial tablet for Bromfield Parish Church, to present a portrait to the Royal Society of Medicine, and to found a Hickman medal for original work of merit in anæsthesia. Subscriptions already received will be sufficient to deal with the three former, but not for the medal. In no better way can the object of this appeal succeed, both in honouring Hickman's name and in serving a useful purpose, than by stimulating research for new anæsthetics and methods, in which it must be admitted British anæsthetists have for some decades rather followed than initiated. The appeal will therefore not be closed for the present in the hope that some who have forgotten or overlooked the matter, or have not appreciated its practical as well as historical importance, and others who may feel that they are indebted to anæsthesia may yet give it their support. A list of subscribers will be published when the Fund is closed; Mr. V. Warren Low, F.R.C.S., 76, Harley-street, W. 1, is the hon. treasurer.—I am, Sir, yours faithfully,

CECIL HUGHES,

London, W., April 3rd, 1929. Hon. Sec.

ACTIVE IMMUNISATION AND DIPHTHERIA.

To the Editor of THE LANCET.

SIR,—I was sorry and surprised to read in the paper by Surg.-Captain P. M. May and Prof. S. F. Dudley on this subject, published in your issue of March 30th (p. 656), that its two distinguished authors decided not to recognise as diphtheria the cases of the two boys, "the appearance of whose throats suggested a diagnosis of diphtheria," and from whose throats virulent diphtheria bacilli were isolated. Suppose these cases had occurred in a group of non-immunised boys, would they then have regarded them as only diphtheria carriers suffering from some other bacterial infection?

Other observers, such as those quoted by the writers, have recognised cases exactly similar to the two referred to above as cases of diphtheria; and in my opinion your two contributors are setting a bad precedent. I venture to say that the slightest attempt

to gloss over a failure, however slight, will lead only to the discredit of the practice of immunisation which they are advocating.

I am, Sir, yours faithfully,

E. W. GOODALL.

Hemingford Abbots, Hunts, April 7th, 1929.

AN OVERDOSE OF THALLIUM ACETATE.

CONFLICTING REPORTS.

To the Editor of THE LANCET.

SIR,—It is interesting to note the conflicting reports regarding dosage and the metric system in this evening's papers when dealing with the thallium acetate case.

The *Star* says: "The strength of the solution, went on Dr. Scovell, was supposed to be 7·8 milligrammes to a drachm of body-weight."

The *Evening News* says: "Miss Tedham said there were 15·4 milligrammes in a gramme."

The *Evening Standard* says incidentally: "... That was based on the rate of 8·5 milligrammes per kilo body-weight," which may be correct.

I am, Sir, yours faithfully,

P. M. KEANE,

London, April 8th, 1929. Squadron-Leader, R.A.F.M.S.

*** A report of the inquest by our medico-legal correspondent follows.—ED. L.

MEDICINE AND THE LAW.

Overdose of Thallium Acetate: An Error in Calculation.

Dr. Cohen, the Wembley coroner, concluded on April 8th an inquiry into the death of three boys who had been treated for ringworm at St. John's Hospital for Diseases of the Skin, Leicester-square. The mother of the three boys described how they had each been given a draught in her presence at the hospital and how they had complained of pains later in the evening and next day and had died at different dates, which she gave. The hospital sister had told her that the medicine might cause the boys to complain of rheumatic pains; for this reason she had not called in a doctor immediately on their complaining of pain. Dr. Spencer Scovell, clinical assistant at St. John's Hospital, gave evidence that the drug used was thallium acetate, a recognised treatment for ringworm, the amount of the drug being based upon the weight of the child. The children had been weighed and the correct dose had been administered, assuming that the solution was of the strength she expected it to be. Asked by the coroner what was the lethal dose, she replied that a man was believed to have died, or very nearly died, after drinking about a gramme of it. The three boys should respectively have had 0·25, 0·23, and 0·18 gramme; that calculation was based on the rate of 8·5 milligrammes per kilo of body-weight. The drug was not dangerous if given in correct doses. Dr. R. M. Bronte and Dr. Roche Lynch gave evidence indicating that death was due to thallium acetate poisoning. Dr. Lynch said the bottle contained 5·6 times the quantity that was on the label. The hospital dispenser, a registered chemist, said she had qualified in July, 1926, and had been at the hospital since May, 1927. She produced the prescription which, as the coroner observed, required a mathematical calculation. Addressing the jury, the coroner said that Dr. Scovell had discharged her responsibilities correctly; it was no part of her duties to make the calculation to check the strength of the contents of the bottle. Thallium acetate, he continued, was a continental drug; the weights of it were worked out on the metric system and required to be converted from metric or decimal weight to apothecaries' weight. In this process a decimal was apparently misplaced; consequently the doses were increased tenfold in strength. The unfortunate error, he said, was one of calculation. The result was terrible, but, at the time the mistake was made, the dispenser was unaware of the danger of an excessive dose. The jury agreed that the three boys died from an overdose of the drug. The coroner then left to them the question whether what had happened was a mere mistake or whether negligence should be attributed to the dispenser for having made the mistake. "Before you can attribute negligence, you must make up your mind that she was not taking due care; this is a mistake in a mathematical calculation, not a careless pouring of a wrong dose from one bottle into another, or taking down a wrong medicine bottle." The jury found as their verdict that death was due to poison accidentally administered; they added a rider that there should be a better system at the hospital of checking weights and measures when making up prescriptions.

A solicitor who appeared at the inquest on behalf of the parents had asked questions which suggested that the treatment was exceptional; the parents' view seems to have been that they should have been specially warned that the drug was highly dangerous, so that they could have decided whether they should allow their sons to have the treatment or not. On this point the evidence of Dr. Bronte and Dr. Roche Lynch was that, though thallium acetate had not been thoroughly investigated, it was a recognised and indeed a common treatment. Similar questions were put on behalf of the dispenser in order to show that she might reasonably have been unaware of the danger of an overdose. The verdict of the jury, delivered after a careful and correct summing-up by the coroner, negatives any charge of negligence, and their rider will no doubt receive attention.

INFECTIOUS DISEASE IN ENGLAND AND WALES DURING THE WEEK ENDED MARCH 30TH, 1929.

Notifications.—The following cases of infectious disease were notified during the week:—Small-pox, 323 (last week 288); scarlet fever, 1919; diphtheria, 1053; enteric fever, 29; pneumonia, 2425 (last week 3578); puerperal fever, 47; puerperal pyrexia, 117; cerebro-spinal fever, 20; acute poliomyelitis, 4; acute polio-encephalitis, 2; encephalitis lethargica, 20; dysentery, 7; ophthalmia neonatorum, 113. No case of cholera, plague, or typhus fever was notified during the week.

Nineteen cases of small-pox were reported from the County of London—namely, Bethnal Green, 3; Poplar, 6; Shoreditch, 2; Southwark, 5; and Stepney, 3. In the vicinity of London an additional 52 cases were reported from West Ham, 1 from East Ham, and 1 from Ilford.

The number of cases in the Infectious Hospitals of the Metropolitan Asylums Board on April 2nd–3rd was as follows:—Small-pox, 163 under treatment, 6 under observation; scarlet fever, 1585; diphtheria, 1811; enteric fever, 9; measles, 98; whooping-cough, 1216; puerperal fever, 20 (plus 6 babies); encephalitis lethargica, 80; poliomyelitis, 4; "other diseases," 62. At St. Margaret's Hospital there were 15 babies (plus 8 mothers) with ophthalmia neonatorum.

Deaths.—In the aggregate of great towns, including London, there was no death from small-pox, 2 (1) from enteric fever, 71 (0) from measles, 9 (2) from scarlet fever, 153 (47) from whooping-cough, 41 (9) from diphtheria, 52 (10) from diarrhœa and enteritis under two years, and 536 (70) from influenza.

The number of deaths from influenza in London is lower than that for any week since that ending Jan. 19th, and the Registrar-General's chart shows that deaths from respiratory diseases in general have come down in almost the same ratio. The death-rate from all causes in the 107 great towns is now down to 17·0, Birmingham and Sheffield, which recently suffered so severely, showing rates of 14·9 and 13·9 respectively. The only towns still attributing a number of deaths to influenza are Bradford 26, Birmingham 24, Manchester and Sheffield 16 each, Bristol 15. Many of the Lancashire towns record 5 or more deaths from whooping-cough, including Warrington, Manchester, and Salford.

The number of stillbirths registered during the week was 311 (corresponding to a rate of 48 per 1000 births), including 67 in London).

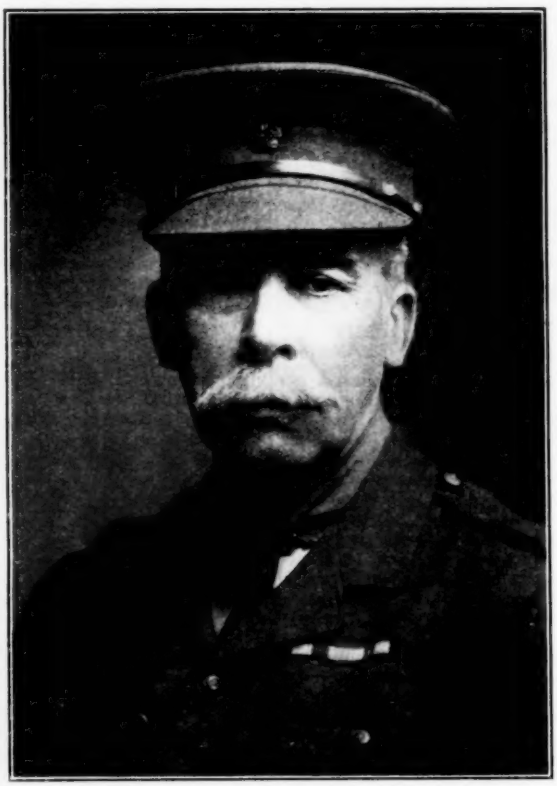
Obituary.

SIR ANTHONY BOWLBY, BART., K.C.B., K.C.M.G., K.C.V.O.,

LATE PRESIDENT OF THE ROYAL COLLEGE OF SURGEONS OF ENGLAND; CONSULTING SURGEON TO ST. BARTHOLOMEW'S HOSPITAL.

WE deeply regret to record the death of Sir Anthony Alfred Bowlby, one of the most prominent figures in our world of medicine, both as a surgeon and as an administrator. The event occurred on Sunday, April 7th, at Stoney Cross, near Lyndhurst, at the age of 73, as a result of pneumonia.

Anthony Bowlby was the son of Thomas Bowlby, a Durham man, who was for a time a London solicitor, but who later led an adventurous life in the Near and Far East, and was on different occasions a special correspondent of the *Times*. Thomas Bowlby died in tragic circumstances in 1860 when in China on his journalistic duties. He was shipwrecked off Point de Galle, and then accompanied Sir James Hope, the English admiral, who was conducting the naval operations against China which followed the breach of the Tientsin Treaty. The conclusion of warfare resulted in the landing of troops at the mouth of Pehtang, and Hope went to Tientsin, where he remained till a treaty was signed in Pekin, but during the operations Thomas Bowlby was taken a prisoner, and died in captivity as a result of the treatment which he received.



SIR ANTHONY BOWLBY.

Photo by Elliott & Fry.

His son, Anthony Bowlby, was then five years old, and he was brought up by his mother, was educated at Durham School, and proceeded thence to St. Bartholomew's Hospital where he duly qualified in 1879 as M.R.C.S. England, proceeding two years later to the F.R.C.S. and filling the house appointments at the hospital. His career as a student was a distinguished one, for he gained many prizes as well as the Brackenbury Scholarship in Surgery. In due course Bowlby became curator of the St. Bartholomew's Hospital museum and completed the catalogue of anatomical, physiological, and teratological specimens, this work being afterwards summarised in his admirable "Students' Guide to Surgical Pathology." As curator he was noted for his intimate knowledge of the specimens and his excellent recollection of many of the clinical histories relating to them. In 1884 he became surgical registrar to the hospital and demonstrator of practical surgery, and in 1891 was elected assistant surgeon on the retirement of Sir William Savory. During his office as registrar he gained the Jacksonian prize at the Royal College of Surgeons of England with a dissertation upon the pathological symptoms and treatment of injuries to nerves, and a few years later he won the Astley Cooper prize with an essay developing the same themes. These two admirable pieces of work were later published in one volume, while in 1887 he delivered the Hunterian lectures at the College of Surgeons along similar lines. He had thus fully justified his election to the staff of the hospital, though he never happened to fill the post of demonstrator of anatomy which at St. Bartholomew's (as at many other of the metropolitan teaching schools) was regarded some 40 years ago as the regular precedent to a staff appointment. But certainly the character of his teaching did not suffer from the omission, for he speedily became recognised by the students as a clear, logical, and forcible instructor, and during the period which followed he built up by his solid work at St. Bartholomew's and at the Alexandra Hospital for Hip Disease a high reputation as an operating surgeon. His clinical teaching was that of a great demonstrator of patients, who combined wide knowledge with a close memory for pathological details. He had a knack of conveying a lesson in a manner that could never be forgotten, as the following extract from a correspondent's letter shows: "My first recollection of Bowlby is a piece of clinical teaching which bit into my memory and never faded. He was going round the wards when he came to a patient suffering from extravasation of urine. After demonstrating the case, he said, in his own inimitable, characteristic, slightly-guttural voice—for he had a little difficulty in pronouncing his 'r's'—'the right thing to do is to make a cut into it, even if you have only got a bit of old rusty hoop iron to do it with.' That sort of teaching was characteristic of the man: eminently practical, simple, and direct, couched in terms which make themselves remembered."

Bowlby's surgery was influenced considerably by Sir Thomas Smith and Howard Marsh, both of whom he had assisted for a very long time. He was never himself regarded as the finest of technicians, nor as a surgeon advancing any particular school of work; in fact, sometimes in his own hospital he was thought to be rather old-fashioned. For instance, he never adopted the method of treating carcinoma of the breast by the sweeping operations which came into vogue in the beginning of this century; he practised himself the smaller local excision, and it is interesting to note that the modern tendency of surgery is with him. His judgment was remarkable. He cared for his patients in every way; he kept them alive, and his opinion was sought always by his colleagues, so that he might have been described as the surgeon to their families.

In 1899 the South African war broke out and Bowlby went to the Cape as chief surgeon in charge of the Portland Hospital, and there laid the foundations of that knowledge of medical-military administration which he later used with such splendid success.

In a book entitled "The Civilian War Hospital" an account was given of the work of the Portland Hospital by Bowlby and the other members of the professional staff—namely, the late Dr. Howard Tooth, Mr. Cuthbert Wallace, Dr. J. E. Calverley, and Surgeon-Major C. R. Kilkelly, the P.M.O. of the hospital. Bowlby describes the sad opportunities offered to the staff to inquire first into the experiences of gun-shot wounds, and, secondly, into the characteristics of epidemic typhoid when the fever began to be serious at Modder River. Bowlby was particularly instrumental in removing camps rapidly from contaminated ground, and the result of his measures of prophylactic hygiene resulted in a remarkable change in the incidence of the fever. In another section of the volume Bowlby and Mr. Wallace (as he then was) give a succinct and detailed description of the surgical work of the war, especially of the surgical aspects of rifle fire, when the warning was issued that the gospel of the innocuous nature of bullet wounds had gone too far, and that there had been too great a confusion between the effects of the penetrating wound made by the projectile and penetrating wound inflicted by sharp instruments. For his services in the South African war Bowlby received the C.M.G. In 1904 he was appointed Surgeon to the Household of King Edward VII., and in 1910 Surgeon in Ordinary to King George, receiving a knighthood.

In 1914 Bowlby received the opportunity for which he was specially fitted. Being at that time a major in the medical branch of the Territorial Force he was attached on mobilisation of our army to the 1st London General Hospital, but his services at G.H.Q. were offered and immediately accepted, and he was appointed consulting surgeon to the Forces with the rank of major-general. The value of his work throughout the war is known to everybody. He became the type of the great medical administrator. He was hard-working, resourceful, clear, and bold. He radiated hope and confidence, while a certain simplicity and generosity of view transformed his abruptness of manner into tactfulness, this being especially displayed in his successful methods of removing friction between the regular and the temporary medical officers—indeed, it is not too much to say that the smooth working between them was largely due to his efforts. His familiarity with the conduct of military medicine gained in the South African war, and his knowledge of hospital administration acquired at St. Bartholomew's Hospital, made of him the ideal counsellor, while his advice always had the admirable backing of first-class professional knowledge. Frequent mentions in despatches were accompanied by the unusual distinction of three knighthoods, for in 1915 he was advanced to K.C.M.G., while in the following year he was appointed K.C.V.O., later C.B., and finally in 1919 K.C.B. In 1923 he was created a baronet.

Bowlby's connexion with the Royal College of Surgeons of England was a long and distinguished one. Winner of the Jacksonian prize and a Hunterian Professor, he was elected to the Council in 1904, and served on that body without break until 1920 when he was elected President in succession to Sir George Makins. He delivered the Bradshaw lecture in 1915 upon Wounds in War, in the course of which he summarised the first year's surgical work as Consulting Surgeon to the British Expeditionary Force in France, compared the conditions in South Africa and France, and described the character of the wounds inflicted by various projectiles with their effects on the tissues. "Nothing has impressed me," he said, "so favourably as the qualities of many of the younger surgeons on whom has rested the chief stress of the actual treatment of the wounded. . . . The care and zeal and patience displayed in efforts to save limbs and life have been no less praiseworthy than the operative dexterity." In this spirit Bowlby always regarded his juniors, and his words are quoted because they illustrate his unceasing aim to establish confidence and justify in the public eye the value that was attached by the high commands to the devoted character of the medical work.

In 1919 he was Hunterian orator at the College and did not experience any of the difficulties which many Hunterian orators must nowadays have in making their words both historical and topical. His address was delivered from the following text written by Hunter himself in relation to his work on bullet-wounds: "My appointment to the Belle-Isle Expedition drew my attention to inflammation in general and enabled me to make observations which have formed the basis of the present treatise." Bowlby proceeded to review military surgery from the time of Hunter in the eighteenth century down to the date of his Oration giving Hunter's and the famous Guthrie's views on primary amputation after gun-shot wound and showing how the percentage of saved limbs had steadily risen. He closed with a brief and clear description of the work of a modern casualty clearing station, showing that the war of movement which characterised the closing stages of the immense campaign just closed had called for the development of new methods. In every way the Oration was alive with topical information, and the audience felt that they were living the life described.

We have attempted to give a description of a great man of affairs, whose keen intellect and strong character showed through every action, while a quiet determination enabled him to carry out what he believed to be the right. For that describes the man.

Sir Anthony Bowlby married in 1898 Maria Bridget, daughter of Canon the Hon. Hugh Wynne Mostyn, and had three sons and three daughters. He is succeeded in the baronetcy by his eldest son, Anthony Hugh Mostyn, who was born in 1906.

ROBERT LAUDER MACKENZIE WALLIS, M.D. CAMB.

Dr. Mackenzie Wallis, who died at Hove on April 1st, at the age of 43 years, was recognised as being in the front line of chemical pathologists. He had never completely regained his health since the serious illness three years ago when he gave up his general hospital work; his death was due to pneumonia and pericarditis following on extraction of some septic teeth.

Educated at Downing College, Cambridge, where he took the natural science tripos in 1908, Mackenzie Wallis devoted himself at first to the study of chemistry, becoming a Fellow of the Chemical Society and demonstrating chemical physiology in the medical School at Cardiff under the late Prof. Berry Haycraft. He then completed his medical education at St. Bartholomew's Hospital, London, qualifying L.S.A. in 1913, and acting as surgical receiving-room officer before he resumed the work more congenial to him of chemical pathologist in the department of bacteriology. This work was interrupted by a period of war service, when he joined the staff of the Welsh General Hospital as temporary captain R.A.M.C. In India,

DR. MACKENZIE WALLIS.

where he was sent, his special merits were soon recognised, and he was seconded from the Corps as a research chemist to the Government of Bombay, where he worked on the purity of anæsthetic agents. Later on he investigated the diastatic output in trench nephritis with a view to elucidating its true nature. Returning at the end of the war he resumed his appointment at Bart.'s until 1926, when he joined the staff of the Children's Clinic, Western General Dispensary, and coöperated in investigations into the biochemistry of the nervous child, in whom he showed the calcium content of the blood to be materially reduced. As a lecturer and teacher of students he enjoyed a good reputation, for he had the essential faculty of stating intricate scientific facts in the simplest language. Side by side with his hospital work he developed a large private practice, in which his special chemical and biochemical knowledge was of great value. He worked particularly at skin sensitisation and the subsequent relief of the toxæmias so detected by the use of vaccines. Biochemical abnormalities in rheumatism, asthma, dyspepsia, and diabetes found in him a competent investigator and therapeutist, and patients came to him from all parts.

One of his colleagues writes: "Mackenzie Wallis was one of the most original thinkers in his branch of medicine. A large amount of routine work did not prevent his speculating on the significance of obscure facts and phenomena; it served him rather as a means for their elucidation. Although in some directions his fertile brain led him astray, in others he achieved a definite advance in work by which he will long be remembered. He was responsible for the hypothesis that the glycosuria of pregnancy is a manifestation of hyperpituitarism—a hypothesis which is now generally accepted. He correlated and defined the value of tests for pancreatic insufficiency; the methods now in routine use for the diagnosis of this condition are accepted largely as the result of his work on their mutual significance. He was responsible also for an original investigation into the pathogenesis of sulphæmoglobinæmia, the results of which indicated that this disease is due to the bacterial synthesis of a reducing substance in the gastro-intestinal tract.

"That Mackenzie Wallis was a tireless worker is sufficiently indicated by the wide field of his original work; that this should have been combined with routine institutional work and practice argued qualities which many must have envied him. His practice, especially in latter years, was a large one, and its success is the best indication of the opinion in which his patients held him. There is no doubt that beyond what he was able to do for them, he was liked by them for some more personal reason. Success in this direction is a thing for which the necessary conditions are hard to define, but the man who deserves it is certainly the man of goodwill and sympathy, and by this criterion Wallis's popularity may well be explained. His good nature was a quality by which all his colleagues will remember him, and he is one of the few men of whom it can be said that he never uttered a harsh word in speaking of anyone."

Dr. Mackenzie Wallis had a very happy family life and was a devoted husband. He leaves a widow and three children to mourn his loss.

ALEXANDER GRANVILLE, C.M.G., C.B.E., M.R.C.S. Eng.

Dr. Granville, who died in London on April 1st after a long and painful illness, had spent the active years of his life as a public health official in Egypt, where he reached the rank of pasha and maintained the high standard of work and conduct which characterised the administration of Cromer and Kitchener.

Alexander Granville came of a Huguenot family and was born at Brighton in 1874. His father died when he was still young, and the boy was taken with his three sisters to Florence, where he attended the day school of Mr. Domeugé, a French refugee, and learned to speak French and Italian fluently. His schooling was completed at Bloxham, in Oxfordshire, whence he entered St. Bartholomew's Hospital, qualifying in 1897. Failing to secure house appointments there for the moment he went on to the West London Hospital as house surgeon and house physician, returning to Bart.'s as resident assistant anæsthetist, a position of some responsibility and of special interest, as gas and oxygen was then just coming into use. While he was holding this post the South African war broke out, and Granville, who as a student had joined the Volunteer Medical Corps, took a commission in this regiment, and was captain before he sailed in 1899. He did good service in the war, obtaining the Queen's medal and three clasps, including Paardeburg; but he contracted enteric fever, complicated by phlebitis, and, returning to duty too soon; the thrombosis which resulted handicapped him throughout life, and was finally responsible for his death at the age of 55 from embolism. The obesity, which was also a legacy of this illness, was a heavy burden of which he made light. Having recovered from his illness he spent some time touring in the Mediterranean and up the Nile in Cook's steamers, and eventually joined the Egyptian army as civil surgeon, from which he was transferred to the public health department of the Egyptian Government. His work in Upper Egypt during the plague visitation of 1907–08 first attracted attention to his energy and administrative powers.

GRANVILLE PASHA.

In 1908, when he was 34 years old, Granville became medical officer of health in Cairo, one of the twenty largest cities in the world, and with a mortality unknown in Europe. A further opportunity soon came to him, for when the Cairo Municipality Section was formed at the Egyptian Ministry of the Interior, he was chosen as its first director, making so conspicuous a success in this post that when the complicated affairs of the Alexandria Municipality were the subject of an inquiry and a change in administration was advised he was appointed director-general there. In 1917 he succeeded Sir Armand Ruffer as President of the International Quarantine Board, a post he held till he retired. During the war, as President of the Board of Conciliation, he did invaluable work during the labour troubles in Egypt, and for his services was created pasha by King Fuad. He was also Red Cross Commissioner for Egypt, Palestine, and Syria from 1917. On retiring from the Egyptian Government service in 1923 his services were retained to attend the meetings in Paris of the Office International d'Hygiène Publique as representative of Egypt. His frequent attendance in Geneva was also required as head of the Egyptian Medical Mission to the League of Nations. It was on one of these journeys from Paris to Geneva that

he had the attack of food poisoning which compelled him gradually to relinquish work, and for the last two years he was able to undertake very little.

Of the personal characteristics which led to a life so full of usefulness one of his friends writes: "Granville made a first-rate administrator because he had the faculty for getting things going, and had a charm of manner which made him popular with everyone from King Fuad down to the humblest peasant. He was a good judge of character, and his conversation was pleasant, kind, instructive, and whimsical. He was a fine linguist; his French was perfect, his Italian good, and of Arabic he had a good working knowledge: in any of them he could be witty.

"He had a keen and critical appreciation of many forms of art: painting and its allies, literature and music, good food and good drink. He wrote amusing letters to his personal friends, illustrating them with sketches and drawings in ink or water-colours, and his powers of burlesque were out of the ordinary. If he had not been a doctor he might easily have become a writer or a sculptor."

His honours were many. He was among other things a Knight of Grace of the Order of St. John of Jerusalem, Officer Legion of Honour, a Commander of the Order of the Crown of Italy, a Commander of the Order of George of Greece, a Commander of the Order of Leopold of Belgium, and a Commander of the Hachimite Order of the Nahda. He received the Second Class Order of the Nile (Egypt), and Orders of Medjidieh and Osmanieh (Turkey). His C.M.G. was granted for his sanitary work in Cairo and his C.B.E. for war work.

He married in 1921 Ierne Goold Adams, daughter of Assheton Biddulph, M.F.H., of Moneygwyneen, Birr, Ireland, who survives him.

WILLIAM LOUIS BYHAM, M.R.C.S. ENG.

THE sudden death of Mr. W. L. Byham on March 19th came as a shock to his many friends and patients in Sunbury-on-Thames and neighbourhood. He had been actively engaged in professional duties during the day on which he died.

Born in Ealing, Byham joined St. Thomas's Hospital as a medical student in 1879. After obtaining his qualifications, he spent three years as a medical officer on board ship, during which time he visited China, Japan, South Africa, and the West Indies. In this country he began practice at Spalding and worked there for seven years; afterwards he took a practice at Sunbury-on-Thames. In 1907 he was appointed medical officer of health to the Sunbury Council in succession to Dr. Palgrave, and amongst other appointments was medical officer to the Staines Union, the Post Office, the Metropolitan Water Board, and the Sunbury Orphanage. During the war he was medical officer to the large depôt of the Royal Army Service Corps at Kempton Park, and did much work for local members of the profession, who were called up for duty with the Forces. It is probable that the strain of this additional work caused his heart to become affected and made it increasingly difficult for him to carry the burden of an important practice, necessitating as it did response to unexpected calls at all times of the day and night, especially during the bitter weather of the past winter. A man of unusually good physique, Byham in his earlier life was known in Rugby football circles as a stalwart forward; he was also a good cricketer and all round sportsman. A colleague writes of him that "although a very busy man during recent years, he was never too much occupied to listen to the story of the poorest patients, and his thoughtful cheery manner endeared him to all with whom he came in contact."

Mr. Byham married in 1894 Miss G. Lamb, of Sunbury-on-Thames, who survives him; he also leaves a son and a daughter. The funeral service on March 23rd was largely attended by friends of all ages.

The Services.

ROYAL NAVAL MEDICAL SERVICE.

Surg. Comdrs. G. A. S. Hamilton to *Constance*: A. G. McKee to *Centaur*: and J. Kirker to *Victory*, for R.N. Barracks, Portsmouth.

ROYAL ARMY MEDICAL CORPS.

TERRITORIAL ARMY.

Col. G. A. Troup, having attained the age limit, retires and retains his rank, with permission to wear the prescribed uniform.

Capt. F. J. Morris to be Maj.

Capt. F. C. Hilton-Sergeant, R.A.M.C., to be Divl. Adjt. 42nd (E. Lan.) Div., and Sch. of Instn., vice Maj. B. C. O. Sheridan, R.A.M.C., vacated.

Lts. to be Capts.: A. H. G. Down, E. J. P. McDowell, and W. G. Saunders.

H. Baxter to be Lt.

Supernumerary for Service with O.T.C.: Lt.-Col. P. H. Mitchiner to be Bt. Col. and Lt. W. R. Martine to be Capt.

ROYAL AIR FORCE.

The undermentioned Flying Officers are granted permanent commissions: D. A. Wilson and F. E. Lipscomb.

Squadron Leader J. R. Crolius (retired list) is reinstated on the active list as a Squadron Leader.

Flight Lt. F. T. Boucher is transferred to the Reserve, Class D. ii.

Brendan Leo Harrington (temp. Lt., General List, Army, Dental Surgeon) is granted a temporary commission as a Flying Officer (Dental) on attachment to the R.A.F.

INDIAN MEDICAL SERVICE.

The undermentioned appointments have been made in India:—A.D.M.S.: Col. P. H. Henderson, R.A.M.C.; D.A.D.M.S.: Maj. R. A. Logan, I.M.S.; Dir., H. and P.: Maj. (Bt. Lt.-Col.) H. H. A. Emerson, R.A.M.C.; A.D.H.: Lt.-Col. A. C. Munro, I.M.S.; D.A.D.H.: Maj. F. C. Tibbs, R.A.M.C.; D.A.D.'s P.: Maj. C. H. K. Smith, R.A.M.C.; and Maj. R. N. Phease, R.A.M.C.

Capt. J. D. O'Neill retires, receiving a gratuity.

Temp. Capt. Chuni Lal Bhola relinquishes his temp. commn.

COLONIAL MEDICAL SERVICES.

Dr. T. W. H. Burne has been promoted to Senior Surgeon, Federated Malay States.

The following appointments have been made: Mr. F. McLagan, Alienist, Gold Coast; Lt. F. O. W. A. Mahon-Daly, Medical Officer, Nyasaland; Mr. R. E. Henderson, Mr. G. H. Henry, Mr. R. C. Jones, Mr. T. Simpson, and Capt. H. R. F. Tweedy, Medical Officers, West African Medical Staff.

DONATIONS AND BEQUESTS.—The late Mr. D. B. Ritchie, of Glasgow, left, subject to certain life interests, £2000 to the Glasgow Royal Cancer Hospital, and the remainder of his estate to the Glasgow Royal Infirmary, the Western Infirmary, and the Victoria Infirmary.

ALCOHOL IN THERAPEUTICS.—Addressing the Society for the Study of Inebriety on April 9th, Dr. J. D. Rolleston said that a remarkable decline had taken place within the last 30 years in the therapeutic use of alcohol. This was best illustrated by the fall in the alcohol bill in various hospitals and was also exemplified by the practice of individual physicians and the small place which alcohol now occupied in text-books of medicine. The low esteem in which alcohol was held as a therapeutic agent in the United States was shown by the fact that only a minority of practitioners applied for a licence in those States in which the right to prescribe alcohol was granted, while a considerable proportion of this minority used it for illicit purposes. Dr. Rolleston said that the conditions in which alcohol was still chiefly employed were pneumonia, enteric fever, diphtheria, and other acute infections, diabetes, heart disease, tuberculosis, senility, and inoperable cancer, but it did not appear to be indispensable in any of them. The experience at the Western Hospital, Metropolitan Asylums Board, of which he is medical superintendent, had shown that in an annual population of over 5000 patients the consumption of alcohol could be reduced almost to nil without any injurious effects. The factors chiefly responsible for the undeserved esteem which alcohol still enjoyed as a therapeutic agent appeared to be extra-medical influences, personal considerations, and tradition rather than scientific evidence.

Medical News.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—The following diplomas have been granted :—

L.D.S.—W. P. Shand, Mary M. Hunter, Elizabeth A. Wilson, Hazel K. Webster, D. A. H. Brown, E. B. Melvin, G. G. Brown, A. K. Samuel, R. L. Allen, C. V. Armitage, P. J. Van Neirop, J. G. Medcalf, A. B. Dickson, and Mark Lessnoff.

UNIVERSITY OF ABERDEEN.—A post-graduate medical course will be held at the Aberdeen Royal Infirmary from April 23rd to June 27th, on Tuesdays and Thursdays, at 3.15 P.M. Particulars are obtainable from the secretary of the University.

UNIVERSITY OF BIRMINGHAM.—Dr. Hector Charles Cameron will deliver the Ingleby Lectures at 4 P.M. on Thursdays, May 23rd and 30th, his subject being Some Types of Septic Infection in the Newly-born ; Dr. Charles Singer will give a course of five lectures on Epochs of Medical History, at 4.30 P.M., on Wednesdays, April 24th, May 1st and 8th, June 19th and 26th ; and Dr. Matthew B. Ray will lecture on the Spa Treatment of Chronic Non-tuberculous Arthritis, at 4 P.M. on Thursday, May 16th. These lectures will all be given at the Medical School Buildings in Edmund-street.

POST-GRADUATE DEMONSTRATIONS AT BIRMINGHAM. A course of post-graduate demonstrations will be given at the General Hospital, Birmingham, on Tuesdays from 3.30 to 5 P.M., and at the Queen's Hospital, Birmingham, on Fridays, 3.30 to 5 P.M., April to July, 1929, beginning on April 23rd at the General Hospital and on April 26th at the Queen's Hospital. The course will include demonstrations on medical, surgical, and gynæcological cases, nervous diseases, ophthalmic cases, diseases of ear, nose and throat, radiology, venereal diseases, and children's diseases.

POST-GRADUATE COURSE ON MENTAL DEFICIENCY.—A course of lectures on mental deficiency and other mental conditions closely allied to it, supplemented by a course of clinical instruction, has been arranged by the University of London Extension Board in coöperation with the Central Association for Mental Welfare, and will be held, in two parts, from May 27th to June 8th. It will be based on the requirements for the University of London Diploma in Psychological Medicine and is intended for qualified medical practitioners, more especially those who are definitely concerned with the care of subnormal and abnormal persons. Communications may be addressed to Miss Evelyn Fox, University Extension Department, University of London, Imperial Institute-road, S.W. 7. Registration fees and applications must be received by May 6th.

BAYLISS-STARLING MEMORIAL SCHOLARSHIP.—This scholarship, founded in memory of Sir William Bayliss and Prof. E. H. Starling, is tenable at University College, London, and is of the annual value of about £120, with exemption from tuition fees. The scholar will be required to follow an approved course of study involving a training in the principles of, and methods of research in, physiology and biochemistry. Candidates must send their applications to the Secretary of University College not later than May 15th.

EUGENICS SOCIETY.—At 5.15 P.M. on Wednesday, April 24th, at the rooms of the Royal Society, Burlington House, Piccadilly, London, Mr. C. J. Bond F.R.C.S., will speak on Hemilateral Asymmetry in Animals and Man and its Relation to Cross-breeding.

ROYAL SOCIETY OF ARTS.—Dr. Leonard Hill, F.R.S., will take the chair at a meeting to be held at the Society's premises in John-street, Adelphi, London, W.C., at 8 P.M., on Wednesday, April 17th, when Mr. F. E. Lamplough will speak on the Properties and Applications of "Vita" Glass.

AUXILIARY ROYAL ARMY MEDICAL CORPS FUNDS.—The annual meeting of the members of these Funds will be held at 2.30 P.M. on Friday, April 26th, at 11, Chandos-street, Cavendish-square, London W., when the officers and committee for the current year will be elected.

UNIVERSITY OF LONDON MEDICAL GRADUATES SOCIETY.—This society will give a complimentary dinner to Lord and Lady Moynihan of Leeds, at the Hotel Metropole, King-street, Leeds, on Friday, April 19th, at 7.15 for 7.30 P.M. The chair will be taken by the president, Sir StClair Thomson. Medical graduates of the University of London who wish to be present should apply to Dr. Rhoda Adamson, 24, Park-square, Leeds, who is acting as local hon. secretary.

GARTON PRIZE AND MEDAL.—A Garton Medal, with an honorarium of £500, will be awarded early in 1932 to the person or group of persons who shall submit the essay embodying the results of original investigations which, in the opinion of the judgesa ppointed by the Grand Council of the British Empire Cancer Campaign, is the best contribution towards the Early Diagnosis of Cancer. Candidates must be British subjects domiciled in the British Empire or Dominions, and the dissertations must embody the results of original investigations carried out, wholly or in part, during the three years immediately preceding the year in which the prize is awarded. It will be seen from our advertisement columns that they should be delivered to the Hon. Secretary of the Campaign, 19, Berkeley-street, London, W. 1, not later than Dec. 31st, 1931.

CLINIC FOR TREATMENT OF RHEUMATISM AT BRIGHTON.—A meeting of medical practitioners in Brighton and Hove was held on April 3rd, to discuss the need for a local clinic for the treatment of rheumatic diseases. Dr. George Morgan (Chairman of the Brighton Division of the B.M.A.) took the chair, and 31 practitioners were present.

Dr. J. Stanley Ellis said that the only way to counter the increasing expenditure on sick benefit, and the appalling waste of time due to rheumatic disability, was to provide early treatment. There was hope of cure or great improvement in 80 per cent. of cases if efficiently treated within the first six months. Far from arthritis being incurable, fewer disease groups responded better to early and proper treatment, and the best way to secure early treatment was by found ng local treatment centres on the lines laid down by the Ministry of Health. The "arthritis unit" work could be done at the existing hospitals, and some in-patient accommodation could also be provided locally, while electro- and hydro-therapeutic treatment needed specially designed institutions. Examples of these could be seen at the new Red Cross Clinic in London, at Wiesbaden, and elsewhere. There was every inducement to start such a centre at Brighton. At present, at the local hospitals, only about 15 per cent. of rheumatic patients were cured or returned to full work, whereas by a special clinic at least 40 per cent. ought to be cured, and a further 30 per cent. enabled to do their ordinary work for nine months or a year before requiring further treatment.

Dr. M. B. Ray, hon. secretary of the National Campaign against Rheumatic Diseases, explained that this Campaign arose from work started nearly four years ago by the International Society of Medical Hydrology. It was now launched as an independent organisation and was to include in its membership representatives of all the various friendly and other societies and associations especially interested in diminishing rheumatic sickness. After speaking of the treatment to be given at the Clinic, including the employment of heat and cold and movement, manipulation and exercises, radiation and electricity, and the need for facilities for research, he went on to say that, if possible, the clinic should be closely associated with a fully equipped hospital department or arthritis unit, where patients could be sent for complete investigation. Removal of infective foci, if desirable, could be done there, and bacteriological and biochemical investigation could be undertaken. The clinic or centre would act as a clearing-house, and those who needed spa treatment would be sent to the particular spa indicated by their condition.

Dr. Duncan Forbes (M.O.H. for Brighton) laid stress on the arthritis unit as of first importance. He hoped that one would be established at the Royal Sussex County Hospital, where all the necessary equipment for team-work was already provided. He advised the establishment by the municipalities of a physical treatment centre which would compare favourably with those already at work in the spas ; if that were not possible, the scheme should be dropped.

After further discussion, a resolution was passed, nem. con., in favour of setting up a clinic in Brighton.

TRELOAR HOSPITALS AND COLLEGE.—On April 5th the trustees of the Lord Mayor Treloar Cripples' Hospital and College at Alton entertained the medical staff to dinner at the Barbers Hall in the City of London. Lieut.-Colonel Frederick Lawson, chairman of the trustees, presided over a gathering which included Miss Florence Treloar, the Lord Mayor of London (Sir Kynaston Studd), the two Sherriffs (Sir William Waterlow and Mr. W. G. Coxen), and the Master of the Barbers' Company (Mr. Leonard Denny). Sir Alfred Robbins, in proposing the toast of the Lord Mayor and Corporation, spoke of Sir Kynaston's long and invaluable services to young people, and in reply the Lord Mayor said how glad he was to be associated with the work for cripples started by Sir William Treloar, his predecessor in office. Colonel Lawson remarked on the appropriateness of holding the dinner in the City, from which the Treloar hospital had always had so much sympathy and support, and especially in the Barbers Hall, which was so closely identified with the history of the surgeon's art. The present year, he said, saw

the twenty-first birthday of Alton, and the record was one to be proud of; for among the 5000 cases which had passed through the institution the death-rate had been under 2 per cent. and 95 per cent. of the children had been discharged with their disease arrested. Mr. O. L. Addison said that before the Alton hospital was established there had been no proper provision for tuberculous cripples, who oscillated between their own homes, the hospitals, and the infirmaries. The revolution it had brought about could only be understood by those who, like himself, were associated with a children's hospital. At Great Ormond-street 25 years ago the wards were swamped by these cases, whose fate it was to be patched up and returned home to relapse; but now, instead of forming the bulk of cases there, they were only a small number, thanks to the Treloar hospital and similar institutions modelled on it all over the country. The grouping of these cases under one man meant that all sorts of improved methods could be initiated and those at Alton had become a standard for the whole world. This success was due to the energy, imagination, and enthusiasm of Sir Henry Gauvain, and no one could have any idea of the value of what he had done. The Master of the Barbers Company, at the chairman's request, gave an account of some of the treasures housed in the hall, which was built in 1643 by Inigo Jones on a site which had been in the Company's continuous occupation since 1308. It had been preserved, he said, during the Great Fire by the herb garden under its walls and since then their priceless possessions had miraculously escaped many dangers to which such things were subject—fire, bombs, burglary, and the American dollar. He drew especial attention to Hans Holbein's picture of Henry VIII. bestowing its charter on the Company, to the portrait of the Duchess of Richmond, which was the original of the figure of Britannia on the penny, and to the several gifts of plate and pictures to the Company by reigning sovereigns of England. Sir James Berry, proposing the health of the trustees, spoke of the great change in the treatment of hip disease since 50 years ago, when it was really pitiable, and Colonel Lawson, in his reply, commended the admirable services of the matron and nursing staff. Sir Henry Gauvain and his assistants, and Mr. H. B. Harper, the secretary.

Among members of the medical staff and others attending the dinner were Mr. H. A. T. Fairbank, Dr. Hugh Thursfield, Dr. I. W. Magill, Dr. F. H. Young, Dr. Gordon Holmes, Dr. N. G. Horner, Sir Cuthbert Wallace, Dr. R. S. Frew, Mr. W. S. Duke-Elder, Mr. Mortimer Woolf, Dr. C. E. M. Jones, Dr. Mackenzie, Mr. F. F. Burghard, Mr. W. T. Holmes Spicer, Mr. T. P. Kilner, Sir Alfred Yarrow, Mr. T. J. Harrowing, and the Rev. C. E. Bond.

Medical Diary.

Information to be included in this column should reach us in proper form on Tuesday, and cannot appear if it reaches us later than the first post on Wednesday morning

SOCIETIES.

ROYAL SOCIETY OF MEDICINE, 1, Wimpole-street, W.

TUESDAY, April 16th.—5.30 P.M., GENERAL MEETING OF FELLOWS. Ballot for election of the Fellowship.

THURSDAY.—5.30 P.M., TROPICAL DISEASES. Paper by Prof. A. Paldrock (Tartu): Observations upon Leprosy in Estonia and its Treatment by Carbon Dioxide Snow and Solganal. (Communicated by Sir Leonard Rogers). Speakers: Dr. F. G. Chandler, Dr. Haldin-Davis, and Prof. J. A. Gunn. Short Paper: Dr. F. G. Rose: A New Method of Obviating Blockage of the Veins in the Intravenous Administration of Sodium Hydnocarpate in Leprosy. DERMATOLOGY, THERAPEUTICS and PHARMACOLOGY: Members of these Sections are specially invited to attend this meeting.

FRIDAY, April 19th.—OBSTETRICS: There will be no meeting of the Section in April. 8.30 P.M., ELECTRO-THERAPEUTICS. Papers: Dr. S. Gilbert Scott: Myeloma—Differential Diagnosis. Dr. J. Duncan White: Bone Lesions in Tropical Diseases.

ROYAL MICROSCOPICAL SOCIETY, 20, Hanover-square, London, W.

WEDNESDAY, April 17th.—7.30 P.M., Dr. P. L. Li: Dr. H.S.D. Garven, and Dr. R. Howard Mole: The Microscopic Anatomy of the Vascular System of the Dog's Spleen.

LECTURES, ADDRESSES, DEMONSTRATIONS, &c.

FELLOWSHIP OF MEDICINE AND POST-GRADUATE MEDICAL ASSOCIATION, 1, Wimpole-street, W.

MONDAY, April 15th, to SATURDAY, April 20th.—LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE Endsleigh-gardens, W.C. Tues. and Thurs., at 2 P.M., Lecture-demonstrations.—ROYAL FREE HOSPITAL, Gray's Inn-road, W.C. Wed., at 5.15 P.M., Lecture-demonstration.—LONDON TEMPERANCE HOSPITAL, Hampstead-road, N.W. 4 to 5.30 P.M., General Practitioners' Course; Medicine, Surgery, and Specialties.—ROYAL WATERLOO HOSPITAL, Waterloo-road, S.E. Medicine, Surgery, and Gynæcology; three weeks' course.—WEST END HOSPITAL FOR NERVOUS DISEASES, 73, Welbeck-street, W. Daily Lecture-demonstrations at 5 P.M., for one month. Further particulars from the Fellowship of Medicine.

NORTH-EAST LONDON POST-GRADUATE COLLEGE, Prince of Wales's General Hospital, Tottenham, N.

MONDAY, April 15th.—2.30 to 5 P.M.: Medical, Surgical, and Gynæcological Clinics. Operations.

TUESDAY.—2.30 to 5 P.M.: Medical, Surgical, Throat, Nose and Ear Clinics. Operations.

WEDNESDAY.—2.30 to 5 P.M.: Medical, Skin, and Eye Clinics. Operations.

THURSDAY.—11.30 A.M.: Dental Clinics. 2.30 to 5 P.M.: Medical, Surgical, and Ear, Nose and Ear, Nose and Throat Clinics. Operations.

FRIDAY.—10.30 A.M.: Throat, Nose and Ear Clinics. 2.30 to 5 P.M., Surgical, Medical, and Children's Diseases Clinics. Operations.

ROYAL NORTHERN HOSPITAL, Holloway-road, N.

TUESDAY, April 16th.—3.15 P.M., Dr. P. O. Ellison: Pathological Investigations.

CENTRAL LONDON THROAT, NOSE, AND EAR HOSPITAL.

MONDAY, April 15th.—1.30 P.M., Examination of the Ear.
WEDNESDAY.—1.30 P.M., Examination of the Sinuses.
FRIDAY.—4 P.M., Mr. N. Rankin: Examination of Cases of Discharge from the Nose.

MANCHESTER ROYAL INFIRMARY POST-GRADUATE CLASSES.

TUESDAY, April 16th.—4.15 P.M., Mr. W. H. Hey: Cancer Diagnosis.

FRIDAY.—4.15 P.M., Dr. A. Ramsbottom: Demonstration of Medical Cases.

ANCOATS HOSPITAL POST-GRADUATE LECTURES, Mill-street.

THURSDAY, April 18th.—4.15 P.M., Dr. Twining: X Ray Findings in Diseases of the Chest.

Appointments.

GALLOWAY, J. C., M.D., Ch.B. Aberd., D.P.H., has been appointed one of the Medical Referees under the Workmen's Compensation Act for Banff County (Sheriffdom of Aberdeen, Kincardine, and Banff).

HAYWARD, E. W., F.R.C.S.E., Principal Medical Officer, Jodhpur State (Rajputana).

City of London Maternity Hospital, City-road, E.C.: GORDON, J. C., M.B., Senior Resident Medical Officer: ALLAN, W. B., M.B., B.S., Assistant Resident Medical Officer.

Queen Charlotte's Maternity Hospital, Marylebone-road, N.W.: STEVENS, I. H. K., M.D. Lond., M.R.C.P. Lond., Senior Resident Medical Officer: JENNINGS, D. R., M.B., Ch.B. N.Z., F.R.C.S. Edin., Assistant Resident Medical Officer.

Certifying Surgeons under the Factory and Workshop Acts:—COLLINS, H. S., M.D., B.Ch.Dub. (Hallingbourne, Kent); WIDGERY, F. W., F.R.C.S. Eng., L.R.C.P. Lond. (Midsomer Norton); and WYPER, J., M.B., Ch.B. Glasg. (Horsmonden, Kent).

Vacancies.

For further information refer to the advertisement columns.

Aberdeen, Royal Aberdeen Hospital for Sick Children.—Two Hon. Asst. S.'s.

Aberdeen Royal Infirmary.—Jun. Asst. Ophth. Surg.

Bethlem Hospital, Lambeth-road, S.E.—Two Res. H.P.'s. At rate of £25 per quarter.

Bethnal Green Hospital, E.—Asst. M.O. £350.

Bethnal Green Metropolitan Borough.—M.O.H. £1100.

Birmingham, City Mental Hospital.—Jun. Asst. M.O. £350.

Birmingham, Ear and Throat Hospital.—3rd H.S. At rate of £150.

Birmingham and Midland Eye Hospital, Church-street.—Surgical Registrar.

Blackburn and East Lancashire Royal Infirmary.—4th H.S. At rate of £130.

Blackpool, Victoria Hospital.—H.S. £120.

Bradford Royal Infirmary.—H.P. and 2 H.S.'s. Each £150. Also Hon. P.

Brighton, New Sussex Hospital for Women, &c.—H.S. and H.P. Each at rate of £50.

Brighton, Royal Alexandra Hospital for Sick Children.—H.P. £100.

Brighton, Royal Sussex County Hospital.—Cas. H.S. £120.

Bristol, City and County of.—Asst. M.O. £600.

Canterbury, Kent and Canterbury Hospital.—Res. M.O. At rate of £125.

Carshalton, Surrey, Queen Mary's Hospital.—Jun. Asst. M.O. £500.

Derby, Brethy Hall Orthopædic Hospital, near Burton-on-Trent.—Res. Med. Supt. £750.

Derby, Derbyshire Education Committee.—Asst. School M.O. £600.

Derby, Derbyshire Royal Infirmary.—H.P. £150.

East Suffolk, Administrative County of.—Asst. County M.O.H. £600.

Evelina Hospital for Children, Southwark, S.E.—H.S. At rate of £120. Also Hon. Phys. to Out-Patients.

Gloucester County Mental Hospital.—Jun. Asst. M.O. £350.

Halifax Royal Infirmary.—Third H.S. At rate of £100.

Hampstead General and North-West London Hospital, Haverstock Hill, N.W.—H.S., Cas. M.O. Also Cas. Surg. O. Each at rate of £100.
Harefield, Middlesex, County (Tuberculosis) Sanatorium.—Third Asst. Res. M.O. £400.
Huddersfield Royal Infirmary.—Locum Pathologist. 12 guineas weekly.
Hull Royal Infirmary.—Cas. H.S. At rate of £130.
Liverpool City.—Asst. City Bacteriologist. £600.
London Female Lock Hospital, Harrow-road, W.—Hon. Obstet. Surg.
London Skin Hospital, 40, Fitzroy-square, W.—Hon. Dermatologist.
Manchester, Ancoats Hospital.—Res. Surg. O. £200.
Manchester Babies' Hospital, Burnage-lane, Levenshulme.—Hon. Ear, Nose and Throat Specialist.
Manchester Royal Infirmary, Central Branch, Roby-street.—Jun. H.S. £100.
Manchester, Salford Royal Hospital.—Res. Surg. O. At rate of £200.
Manchester, Victoria Memorial Hospital.—Sen. H.S. £250.
Metropolitan Hospital, Kingsland-road, E.—Sen. H.P. and H.S., Jun. H.P. and H.S. Also two Cas. O.'s. Each at rate of £100.
Miller General Hospital, Greenwich-road, S.E.—Out-Patient Officer. At rate of £150.
New Delhi, India, Lady Hardinge Medical College.—Prof. of Anatomy. Rs. 750 a month.
Northern Rhodesia, Roan Antelope Copper Mines.—Chief M.O. £2000.
Preston and County of Lancaster, Queen Victoria Royal Infirmary. Hon Asst. S. and Hon. Asst. P.
Prince of Wales's General Hospital, Tottenham, N. — Res. Sen. H.P. Sen. H.S. and Special H.S. Each at rate of £120. Also Jun. H.P. and Jun. H.S. Each at rate of £90.
Queen's Hospital for Children, Hackney-road, E.—Surg. to Ear, Nose and Throat Dept. Cas. O. At rate of £100. Also H.P. At rate of £100.
Redhill, Surrey, Royal Earlswood Institution.—Jun. Asst. M.O. At rate of £250.
Royal College of Surgeons.—Examiners, &c.
Royal Waterloo Hospital for Children and Women, Waterloo-road, S.E.—H.S. At rate of £100.
St. Andrew's Hospital, Dollis Hill, N.W.—Jun. Res. M.O. £120.
St. John's Hospital, Lewisham, S.E.—Res. M.O. £200. Also Res. Cas. O. and Jun. H.S. Each at rate of £100.
St. Stephen's Hospital, 369, Fulham-road, S.W.—4th Asst. M.O. £300.
Samaritan Free Hospital for Women, Marylebone-road, N.W.—H.S. At rate of £100.
Sheffield, Nether Edge Hospital.—H.P. £150.
Sheffield Royal Hospital.—H.P. Also Res. Anæsthetist. Each at rate of £80.
Southend-on-Sea, County Borough of.—Asst. M.O £600.
University College, W.C.—Bayliss-Starling Memorial Scholarship. £120.
Warrington Infirmary and Dispensary.—H.P. £150.
Westminster Hospital, Broad Sanctuary, S.W.—Asst. Surg. Reg. At rate of £50.
Wolverhampton Poor-law Institution.—Sen. Res. M.O. £600. Also Jun. Res. Asst. £200.
Wolverhampton and Midland Counties Eye Infirmary.—H.S. £200.
Wolverhampton, Royal Hospital.—Cas. O. and Res. Anæsthetist. At rate of £125.

The Chief Inspector of Factories announces vacant appointments for Certifying Factory Surgeons at Wolston (Warwickshire) and Irlam (Lancs).

Births, Marriages, and Deaths.

BIRTHS.

DODD.—On Easter Day, at the Red House, Dartmouth-grove, S.E., the wife of Dr. Frederick H. Dodd, of a son.
SHEPHERD.—On Easter Sunday, at St. Andrew's-crescent, Cardiff, the wife of Dr. C. W. Shepherd, of a daughter.

MARRIAGES.

MOORE—HOLT.—On April 4th, at St. Barnabas, Kensington, Frederick Craven Moore, M.D., F.R.C.P., of Victoria Park, Manchester, to Marjory, second daughter of the late Sir Edward Holt, Bart., and Lady Holt, of Manchester.

DEATHS.

ADDISON.—On April 3rd, at Worthing, very suddenly, Hugh Cecil Addison, L.R.C.P. Lond., M.R.C.S.
BOWLBY.—On April 7th, at Stoney Cross, near Lyndhurst, Sir Anthony Alfred Bowlby, Bt., D.C.L., K.C.B., K.C.M.G., K.C.V.O., F.R.C.S., aged 73 years.
DUHIG.—On April 3rd, 1929, at Heckmondwike, Yorkshire, after a very short illness, David John Duhig, M.D.Trin. Coll. Dub., Fellow Royal Society of Medicine; Hon. Assistant Aural Surgeon, Dewsbury Infirmary. Deeply mourned by his sorrowing wife and family. "Love outlasts death."—R.I.P.
GILLIES.—On April 3rd, at Stafford-road, Southsea, J. W. F. Gillies, M.R.C.S. Eng., L.R.C.P. Lond., of Down-street, S.W.
VAISEY.—On April 2nd, at Combe Down, Bath, Thomas Frederick Vaisey, M.R.C.S.E., L.R.C.P., late of Winslow, Bucks.
WALLIS.—On April 1st, at Hove, Robert Lauder Mackenzie Wallis, M.D., of Harley-street, W., aged 43 years.

N.B.—A fee of 7s. 6d. is charged for the insertion of Notices of Births, Marriages and Deaths.

Notes, Comments, and Abstracts.

PITFALLS IN THE RIGHT SIDE OF THE ABDOMEN.*

BY H. W. CARSON, F.R.C.S.,
SENIOR SURGEON TO THE PRINCE OF WALES'S GENERAL HOSPITAL

EVERY surgeon recognises the difficulty of abdominal diagnosis, but we are all agreed that there are many more difficulties on the right side than on the left. When you think of the possibilities of error in left-sided abdominal diseases you see how few they are. It is true one may miss an early stomach cancer, one can mistake a spleen or a kidney for a colonic tumour, one may not realise how often a subacute appendicitis gives pain in the left iliac fossa or even the left hypochondrium. Diverticulitis may be difficult to diagnose and a left ureteric stone may require some study, but these are trifles compared with the right-sided pitfalls.

This is probably due to the protean activities of the appendix, and from the purely vicious, if unconscious, association of right-sided abdominal pain with disease of that organ. When we consider that until 30 years ago it was never suggested that in its quiescent state between attacks the appendix could give rise to symptoms, it is amazing how widespread is the belief that it is responsible for so many troubles. But in addition to the appendix the right side of the abdomen has many traps for the unwary and for the most skilful. Diseases of the gall-bladder are traditionally difficult to diagnose, and its close association with the duodenum, anatomically, perhaps, rather than pathologically, makes confusion easy between disorders of these neighbouring structures. Can we be sure of differentiating between those organs by the history, by the symptoms, by our abdominal examination, or by the exactitude of the ancillary methods of survey?

Two years ago or so my friend Dr. J. M. T. Finney, recently Professor of Surgery at Johns Hopkins University, Baltimore, visited at short notice my operation clinic at the Prince of Wales's General Hospital. I hoped to induce him to do his operation of pyloroplasty for duodenal ulcer, and did my best to obtain a case of duodenal ulcer off my list. The only case I could get in was a rather doubtful one, and when Dr. Finney and I went over the symptomatology and X-ray films, we were both unwilling to give a positive diagnosis of duodenal ulcer. He suggested that I should open the abdomen, and if it proved to be a case of duodenal ulcer he would do his operation. Exploration showed the case to be one of gall-stones, and Dr. Finney laughingly said: "It is delightful to come all these miles to see the same mistakes that I make myself!"

Duodenal Ulcer or Gall-stones?

In my experience, one is more apt to diagnose a cholecystitis as a duodenal ulcer than a duodenal ulcer as a cholecystitis. What are the points one relies on? Both those conditions tend to have periods of comparative freedom from symptoms. I am sure that the severe attacks of gall-stone colic are more severe and less amenable to treatment than the severe attacks of duodenal ulcer. I know that sometimes the duodenal ulcer patient will give a very lurid account of his sufferings, and I have seen patients in a bad attack obviously in great pain, but it does not compare with the true gall-stone colic which will cause vomiting, sweating, and collapse, and for which there is no remedy but morphia. But it is the quiescent period, or perhaps one should say in the semi-quiescent period, that real difficulty arises.

In making my preliminary diagnosis before I decide what ancillary investigations should be made, I rely on three points: (1) the history of the attacks; (2) the symptoms during the intervals (the duodenal case is generally quite well unless the appendix is also affected, while the gall-bladder often has flatulent dyspepsia and right shoulder aching); (3) the examination of the abdomen (comparative rigidity of the upper right rectus muscle in duodenal ulcer compared with the same condition of the upper oblique muscles), and Murphy's sign in gall-bladder. Murphy's test consists of an examination of the gall-bladder with the patient sitting up. The surgeon sits behind the patient and, placing his hands on the right and left hypochondria, directs the patient to relax his muscles and take a series of deep breaths. With each expiration the hands are pressed into the hypochondria, the palms of the hands being brought more and more horizontal—after three or four breaths the gall-bladder will be brought down during inspiration on

* Being a post-graduate lecture delivered before the Fellowship of Medicine on March 18th.

to the fingers of the right hand, and if it is tender there will result a characteristic catch in the breathing. The test differentiates admirably between gall-bladder and kidney affections.

One must not put too much reliance on physical configuration, although one is naturally inclined to consider the fair, fat-and-forty matron a more likely host of gall-stones than the thin fine-drawn male, nor must one expect too much help from the patient's likes and dislikes in food.

Special Methods of Investigation.

What of the ancillary methods? Examination by X rays has taken the foremost place in both cases. Both have their limitations. I think it will be agreed that radiographic examination after a barium meal does not give as high an average of successes in duodenal as in gastric ulcer. This is due to the fact that the great majority of duodenal ulcers are superficial—that is, there is no crater in which the barium can lodge; while in lesser curve ulcers, at any rate as the surgeon sees them, a crater or a bud is the rule. Craters are rare in duodenal ulcer unless the ulcer is on the posterior or inner surface, and these form quite a small proportion. And then the shape of the duodenal cap may be distorted by spasm due to many things, among them cholecystitis. I have under my care at the moment a medical man who has attacks characteristic of duodenal ulcer, with marked deformity of the cap, in whom symptoms occur only in association with phosphaturia and oxaluria. In only two respects does he differ from an ordinary duodenal ulcer; he vomits incessantly during the attack, and he has no hyperchlorhydria. The examination of the gall-bladder by X rays after the administration of the dye is still in its infancy, and has not yet given me the proportion of successful diagnosis which I consider necessary if I am to rely on it, nor is it yet decided whether the dye should be injected intravenously or given by the mouth in a cachet.

The Graham Cole test consists in the administration of 3 to 5 grammes of tetraiodophenolphthalein intravenously, in two doses of 35 to 50 grains in kerasol capsules by the mouth. The preliminary preparation of the patient is most important. The gall-bladder is examined radiographically at varying intervals, beginning four hours after the injection, or 12 hours after the oral administration, and examinations are repeated several times during the next 24 hours. A healthy gall-bladder casts a shadow which becomes gradually smaller and more concentrated, and finally disappears.

The other method is the chemical examination of the stomach contents in duodenal ulcer, and the microscopical and chemical examination of the duodenal contents in gall-bladder disease.

I am afraid we are all rather disappointed with the test-meal as a method of clinching the diagnosis. When the fractional test came in, we all hoped great things of it, and the curves certainly looked very instructive, but further experience shows such wide variations in the consecutive examinations that one has begun to lose faith in it. Perhaps the most helpful examination is that of the resting juice which may show variations, both chemical and microscopical, which may be very useful. The examination of the duodenal contents by Vincent Lyon's method has never really caught hold of English investigators. I was in Philadelphia last December, and had the great pleasure of seeing my friend, Dr. Lyon, at work. His method consists in the introduction directly into the duodenum by means of the Rehfuss tube of 50 c.cm. of a 25 per cent. solution of magnesium sulphate. This gives rise to a rapid discharge of bile, which is then aspirated through the tube. Lyon differentiates between the A bile, first to come, from the common bile-duct, the B bile, second to come, from the gall-bladder, and the C bile from the hepatic ducts, which comes last. In some patients, 15 c.cm. of melted butter, or 30 c.cm. of cream and egg yolk give equally good results.

He showed me some strange things, and there is no doubt that quite a deal of information is forthcoming from this method of investigation both in gall-bladder disease and duodenal ulcer, and there is no doubt it will make its way.

At one time I thought I proved to my own satisfaction that *Bacillus coli* cystitis was often associated with gall-stones, but it is only a chance happening, I believe. Also, we hoped that we might find an excess of cholesterol in the blood, but this has also come to nothing.

Symptoms arising in the Urinary Tract.

My reference to oxaluria may excuse a digression to refer to the very baffling symptoms that this condition can give rise to. My first experience was some 25 years ago, when I dared to disagree with that very eminent surgeon, Mr. C. J. Bond, of Leicester, over the diagnosis in the case of a well-known master of hounds. My diagnosis, which was of appendicitis, carried conviction against Mr. Bond's diagnosis of a minute ureteric stone, and I operated, and have still on my desk an ink-stand given to me by my grateful patient. I sent him away on a sea voyage, and while he was in the West Indies he had a similar attack to the old ones and passed a minute oxalate stone. He sent it to me with a cheery letter. The ink-stand is a constant check upon any desire I may have to consider myself infallible.

The last case occurred some two years ago, when I was called upon to see a man who had apparently a severe attack of intestinal obstruction. He was collapsed, vomiting, distended, and all the rest of it. I explored him and found nothing except generalised intestinal distension. I advised the doctor to keep a sharp look-out for the passage of a urinary stone. For three or four days his life seemed to hang in the balance, but he recovered, and 14 days after his seizure he passed an oxalate stone and has remained well. And that brings me on to the subject of the differentiation between the appendix and some renal lesions.

The acute infections are more easy than the chronic recurring attacks. I do not think one ought to mistake a perinephric abscess of hæmatogenous origin for a retrocæcal appendix abscess. The former is never so acute, and rarely leads to an abdominal mass. But to distinguish between a retrocæcal appendicitis and acute ascending pyelitis of pregnancy may be very difficult, especially if the kidney is not functioning, so that pus does not appear in the urine. The most valuable signs of pyelitis are: (1) acute tenderness in the costovertebral angle, (2) an initial rigor, and (3) a temperature perhaps as high as 104° F., but certainly higher than is usual in acute appendicitis. Dietl's crises (an intermittent hydronephrosis due to kinking of the upper ureter) may lead to an error, but there is rarely any need for hurry in those cases, and a pyelogram will settle the diagnosis without difficulty.

Appendicitis.

There is the old warning of the danger of mistaking a perforated duodenal ulcer for an acute appendicitis on the grounds that the duodenal contents tend to gravitate to the right iliac fossa and give rise to signs in the appendix area. I am sorry I cannot subscribe to this opinion of difficulty. Even in the absence of a previous history of duodenal indigestion, the onset, the general character of the abdominal rigidity, and especially the condition of the patient, all tend to make the differentiation easy, and I do not think the mistake should be made, nor is it, I believe, made very often. But I will tell you of an exercise which will help you. In any case where I suspect an acute appendicitis, I always set myself and my house surgeon the task of stating the exact position and appearance of the appendix before I operate. As experience accumulates one gets nearer and nearer to the truth, and I have found it particularly valuable in diagnosing the acute retrocæcal appendix which is always the most difficult.

Among the more chronic lesions, the differentiation between appendicitis and ureteric stone may be very difficult if for any reason the stone cannot be localised with X rays. One has then to rely upon the possible occurrence of urinary symptoms, the presence of abnormalities in the urine, and a cystoscopic examination. That many mistakes are made is evidenced by the number of cases of kidney and ureteric stone we see in which the appendix has already been removed without relief. They come to a high proportion of the cases. The only safeguard is that which results from our hospital system where every patient passes through many hands before the diagnosis is definitely settled.

The Distinction of Pain and Tenderness.

Perhaps the greatest difficulty of all, however, is to make a correct diagnosis in the common case of a patient complaining of right iliac fossa pain. Here I would like to draw a distinction between pain and tenderness. Conditions giving rise to tenderness are much more easily diagnosed than those giving rise to pain, for pain is purely subjective and varies in significance according to the sufferer's make-up.

Three girls consult you, and each give a story of vague diffuse abdominal pain confined to the right side. The first is apparently in excellent health, you can make nothing out in examination, but you get a history that she has been vigorously engaged in some sport such as lacrosse or basket-ball, or lawn-tennis, all designed to put a strain on the right lower abdomen. You suspect a strained external oblique, or even a commencing hernia. The second is equally healthy. She tells you that last October she had a rather severe attack of abdominal pain, perhaps with vomiting, that she had to lie up for a week or so, and that she still gets occasional discomfort in the right iliac fossa. You suspect an attack of appendicitis which has not entirely subsided. The third is perhaps not quite so healthy or active, and on cross-examination she admits that the pain has been there for a long time, that it gets worse as the day goes on, but is relieved by lying down, that she is tired at night, and constipated. You suspect enteroptosis, and find confirmation on examining her general physique and

noting the skeletal changes, the loss of weight, the muddy complexion, the circulatory abnormalities which characterise this most common and distressing malady.

It was Dickens, I think, who drew a word-picture of the woman who is fated to be killed by her husband, and this picture is a perfect reproduction of the enteroptotic woman.

Enteroptosis.

I am often asked whether X rays are a help in the diagnosis of appendicitis or enteroptosis. The answer is, that they will help but their value must not be exaggerated. It used to be said that a pathological appendix was evidenced (1) if the barium entered the appendix and remained there for a long time, thus showing that the peristaltic power of the appendix was diminished by fibrosis of the wall, or (2) if the barium did not enter at all, thus showing obstruction of the lumen. But now all are agreed, I believe, that no radiological opinions are to be expressed unless the appendix is visualised. If it is, some opinion can be passed as to whether it is tender—a rather doubtful point—or whether it is abnormally fixed. Enteroptosis, or at any rate a pathological hypermobility of the colon, is also very difficult to estimate by X rays. Everyone of my age was taught that the hepatic flexure was up under the rib, and the caput cæci above the level of the pelvic brim. We know now that in the erect position in health the hepatic flexure is rarely much above the intercristal line, and the caput cæci is quite often in the true pelvis. The same is true of the transverse colon, which, instead of passing obliquely across the umbilical region up to the splenic flexion, much more often sags in the middle almost into the pelvis. What, then, are the radiographers' evidences of a pathological enteroptosis? They may be summed up as evidence of abnormal fixation and delayed function. If the cæcum or transverse colon are abnormally placed and fixed, that is pathological; and if the barium remains too long in the lower ileum or cæcum, this is pathological.

There is one justification for an aphorism which I permitted myself when talking about the operative treatment of intestinal stasis, that it is more surgical to free abnormally fixed organs than to fix abnormally free organs.

Tuberculous Lymphadenitis.

Symptoms which one may confuse with those of the chronic appendix are caused by tuberculous mesenteric glands. These are generally seen in children, though they may occur at any age. They give rise to a characteristic train of symptoms—of which colicky pain is the most important—which are now well recognised since I first brought them before the profession in 1918. When I was in Toronto, in December, I was told that so thorough was the control of the milk supply that these cases hardly ever occurred. However, they are still frequent, though I think less frequent than they were in London, their incidence having fallen in common with all forms of surgical tuberculosis. A good deal of discussion has centred round the question of whether chronic appendicitis does occur and cause symptoms in children. I have no doubt of it myself, and I am not alone in thinking that some, at least, of the intestinal indigestion so common in children is due to lesions of the appendix. Generally, however, in children, especially in little children, localisation is not very exact, and the patients seem to complain of pain in the umbilical region rather than in the right iliac fossa. Of all forms of interval appendicitis in children, the mucocele gives rise to symptoms most closely resembling those of tuberculous mesenteric glands.

Finally, I might perhaps suggest that we should all make fewer mistakes in diagnosis in right-sided abdominal lesions if we were not obsessed by the ever-present shadow of the appendix.

LOCAL AUTHORITIES AND MATERNAL DEATHS.

To facilitate inquiry into the causes of mortality in childbirth, local authorities having charge of maternity and child welfare may wish to obtain particulars of maternal deaths occurring in their areas, and the Ministry of Health has been in consultation with the Registrar-General as to the best method of procedure. Reports received by the Registrar-General indicate that some difficulties are being experienced both by local authorities and by registrars of births and deaths in establishing satisfactory plans for the provision of early information respecting the occurrence of maternal deaths. It is understood that in some cases registrars of births and deaths are being asked to identify "maternal deaths" in the sense of deaths due to puerperal sepsis and other diseases of pregnancy and parturition. This general grouping comprises over 150 individual causes of death, as enumerated in the Registrar-General's Manual, and the burden of watching for the appearance upon medical certificates of any of these separate causes is one which, in the opinion of the Registrar-General, registrars cannot properly be expected to undertake. Moreover, even if it were possible for this task to be performed without prejudice to the performance of the registrar's normal duties, local authorities would not thereby secure the complete notification of all "maternal deaths," since certifying practitioners often employ an alternative terminology for many of these causes which could not be identified without medical knowledge.

On these grounds the Registrar-General is disposed to deprecate any such arrangement between a local authority and a registrar of births and deaths. It appears to him that the final identification of deaths as falling within the definition of "maternal mortality" is one which can only be made by persons with medical knowledge, and that this selection must necessarily take place after the receipt of the material by the local authority. Where the local authority already obtains complete returns of all deaths under the provisions of Section 28 of the Births and Deaths Registration Act, 1874, or is now prepared to obtain complete returns for the service of its public health administration in regard to both maternal mortality and other matters, no further question will arise. But where the local authority desires information for the purpose of maternal mortality only, and has no other object in view which would justify the provision of complete returns, this purpose would be adequately served by arrangements for the notifications of deaths of females between, say, 15 and 45 years of age.

This section of the death registers would be sufficient to enable the proper selection of maternal deaths to be made therefrom, and the Registrar-General is not at present aware of any other practicable criterion which would meet the purposes in view.

ULTRA-VIOLET APPARATUS.

THE sixth edition of the "Arnold" ultra-violet and other apparatus issued by Messrs. John Bell and Croyden is a useful publication. It contains illustrations, descriptions, and price-lists of a considerable variety of sources of ultra-violet, luminous, and infra-red radiation, together with a detailed account of accessory gear used with these forms of therapy. The protective goggles used in all light clinics should be tested for their transparency to ultra-violet radiation, for many a black glass lets these rays through. The particular goggles illustrated here are, we believe, safe varieties, and those shown on p. 30 are inexpensive and very suitable for hospital work. Mention is made of a useful kind of garment which can be worn during exposure of the body to ultra-violet. This material consists of a mixture of pure wool and artificial silk, which is said to pass approximately 50 per cent. of the ultra-violet; the openness of the mesh may be mainly responsible for this transmission.

UTERINE FIXATION BY TRANSPLANTED FASCIA.

THE operative treatment of retroflexion of the uterus entails certain disadvantages. The Alexander-Adams method, that of shortening the round ligament, avoids adhesions, but the ligament is apt to stretch in women who have to carry heavy weights. Dr. N. A. Podkaminisky, of the Ukraine National Institute of Industrial Pathology and Hygiene, Charkov, suggests an operation which will fulfil the two requirements of permanence and the avoidance of adhesions without altering the length of the round ligament. He proposes to transplant two strips from the fascia lata into the abdominal cavity and attach them to the ends of the round ligament, suturing them along its whole extent. By this means there should be no displacement of the organs in a small pelvis. Observations from the use of strips of fascia for other purposes show that they readily unite with their new neighbours and lose no elasticity or vascular function; they receive, in fact, an additional supply of blood through the new vessels of the scar-tissue. The author is satisfied with the results of the operation, which are to be communicated later.

ROBB'S DIETETIC BISCUITS.

WE have received from Messrs. Robb and Co., Ltd., Nursery Biscuit Factory, Atkins-road, Clapham Park, London, specimens of their well-known productions, including oatmeal biscuits, wheatmeal biscuits, water biscuits, for general use with butter, cheese, and fruit; Bath Oliver biscuits, recommended for indigestion and table use; ginger nuts, rusks of various kinds, and dietetic biscuits, together with their food biscuits for infants. The productions of this firm, which are manufactured with due regard to the requirements of infants and invalids, are palatable and easily digestible, and find a place in many households. The firm will send trial samples to medical men or nurses on application.

Dosage of Isopral and Hedonal.—Dr. A. E. Beryl Harding writes that the dose of isopral and hedonal recommended by Lambert (THE LANCET, March 2nd, 1929, p. 433, col. 1), as a preliminary injection in the anæsthetisation of cats, should have been given as *0·15* (not 1·15) c.cm. per kg.